ATLAS OF
CUTANEOUS MORBID HISTOLOGY

JOSEPH AND VAN DEVENTER

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CONSISTING OF FIFTY-THREE COLOURED FIGURES
ON TWENTY-FOUR PLATES
AND TEXT

BY

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TO

PROFESSOR DR. O. LASSAR

PROFESSOR AT THE UNIVERSITY OF BERLIN

RESPECTFULLY DEDICATED

BY THE AUTHORS

PREFACE

In the histological atlas which I published in collaboration with my colleague, P. Meissner (Berlin, 1899), we have portrayed such typical examples of skin diseases as, without retouching, were most suitable for photographic treatment. This method has obviously both advantages and drawbacks. A recommendation certainly is that that alone is seen which is actually present in the specimen. On the other hand, it must be admitted that, at the best, but a small portion of the typical specimen can be reproduced by the photographic process, and the most delicate details are altogether ruled out.

Hence I desired, by the employment of up-to-date methods, to portray in a second atlas and by means of coloured plates the several characteristic details of cutaneous diseases. But this proved an exceedingly difficult task, for it was above all things necessary for the plates to be executed by one who was not only a medical man, but also an artist.

Among a large succession of pupils with whom I occasionally discussed the scheme, and some of whom made efforts to carry it out, I met at last Herr J. B. Van Deventer, Oberstabsarzt of the Netherlands East Indian Army in Batavia, who appeared to me quite exceptionally qualified to accomplish the design. My colleague combined the most painstaking industry with great artistic gifts, and with a power of delineating the most difficult details. In a remarkably short time he had prepared the accompanying plates, and I trust that the admirable way in which he has performed the task will meet with well-merited approval.

Thus it only remained for me to write the explanatory text. I have endeavoured to do this in such a way as to include a sketch of the present state of our knowledge of each disease delineated in the plates. I have for other reasons been unable to adopt an alphabetical arrangement of the subjects treated, for the exigencies of space rendered it necessary to arrange the plates in such a manner as the nature and form of the figures depicted permitted.

The preparations are taken from my own collection. To the courtesy of my friend and former assistant, Dr. Dreyer of Cologne, I am indebted for permission to portray nævus congenitus, and to my colleague Peter of Königsberg-in-Pr. I owe my thanks for permission to produce the figure of lymphangioma; my former pupil, Professor Dohi of Tokio, kindly allows me to depict tricho-epithelioma.

We trust that this atlas will serve to attract fresh workers to the study of histology, which is such an indispensable requirement of dermatology.

Berlin, *June* 1906.

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Plate I. Fig. 1. **Acanthosis nigricans.**

× 105, Leitz, Obj. 3. Ocul. 4.

r = rete, g = vessels, b = connective tissue, p = papillary layer, strc = stratum corneum, strg = stratum granulosum.

The most prominent feature of this disease, and that from which it derives its name, is the presence on the skin and mucous membranes, at their point of junction with the skin, of acuminate papilliform elevations which are for the most part distributed diffusely over the larger portion of the cutaneous surface. The preparation from which the section is taken is from the forehead of a patient suffering from the malady. An exhaustive histological examination proves that the acuminate elevation is not formed by a proliferation of the cells of the rete, but that the lesion is the result of hypertrophy of the epidermis. Hence it follows that Kaposi was fully justified in describing by the name of *Keratosis nigricans* the microscopical appearances of this disease, instead of employing the term Acanthosis. An examination of the figure will render it clear that the prominence due to the hypertrophy of the epithelium corresponds to a similar elevation of the layer of prickle cells. And, inasmuch as we hold with the maxim, *denominatio fit a potiori*, we should preferably therefore make use of the term Keratoma. But the employment of the older terminology has become so general that it is not possible to effect a change.

The isolated horny proliferation of the epidermis is distinguishable from the somewhat similar appearance in Icthyosis hystrix by the fact that, in this case, no symmetrical epidermic layers are met with, but in many localities parakeratotic epidermic cell masses are present. These are distinguished by the fact that, contrary to the partially dead, non-nucleated cells of the stratum corneum, they display well-developed nuclei. In that portion of the accompanying figure which is coloured red the prominent nuclei supply evidence of an abnormal hardening, of parakeratosis. The rete is relatively less markedly the seat of proliferation and displays but little keratohyalin, whilst in the papillary layer, so far as can be detected in this portion, which has been removed by the sharp spoon, no trace of infiltration, but merely some dilated capillaries, are found.

On the contrary, in other localities, where the disease has penetrated more deeply, a pronounced pigmentation in the stratum cylindricum suggests the appearances met with in nigricans; these resemblances are present in the form of numerous round or polygonal pigment cells, met with even in the upper portion of the cutis vera. Finally, in the locality last mentioned the fixed connective tissue cells are observed to be increased both in number and size, and a slight cell proliferation is detectable in the adventitia of the papillary and sub-papillary layers. Further, a moderate number of mast cells is detectable, whose granulations are frequently found to be broken down and scattered in the area occupied by the cells.

Plate I. Figs. 2, 3. **Hydrocystoma tuberosum multiplex.**

× 480, Obj. 6, Ocul. 4. × 680, Oil immersion $\frac{1}{12}$, Ocul. 2.

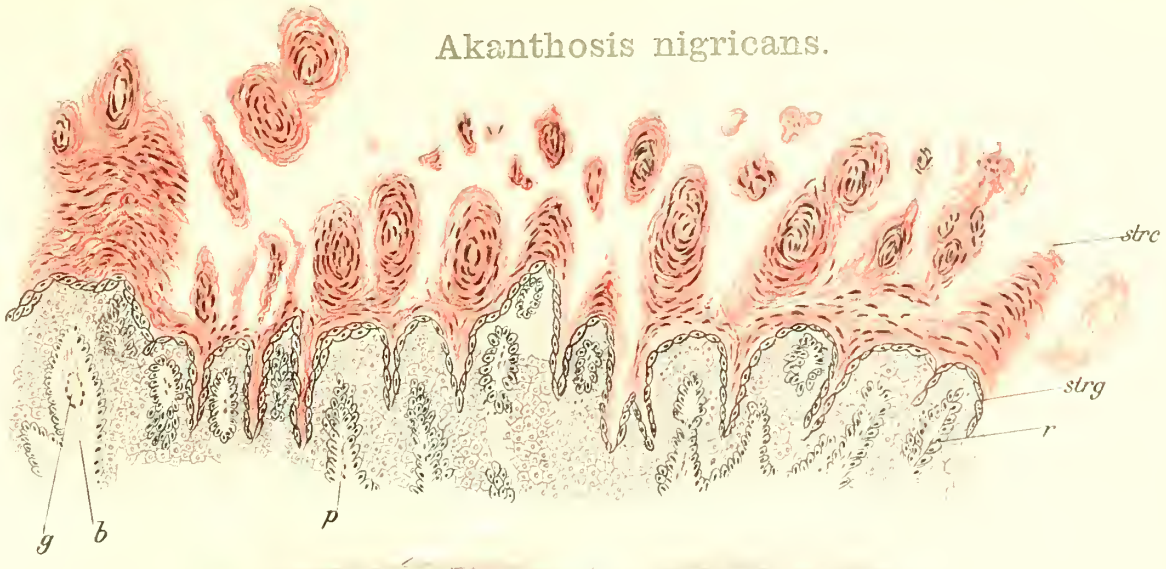
f = fibrin, c = cyst, mk = muscle nuclei, g = vessel, b = connective tissue, r = rete, strc = stratum corneum.

It can only be owing to the rarity of this malady that every fresh observer thinks it necessary to describe it by a new name. From the anatomical standpoint it is interesting to recall the fact that Kaposi, relying on the investigations of Biesadetzki, thought that he had to deal with a disease of the lymphatics (Lymphangioma tuberosum multiplex), and later observers hold that colloid degeneration is in question (Kromayer). Further, it was thought that not merely the lymphatics, but also the blood-vessels were involved, and that the lesion was a Hæmangiomaendothelioma (Wolters and others). But there can be no doubt that, in the cases observed by J. Neumann, Gassmann, and others, the sweat glands were chiefly involved.

The figure represents the preparation taken from a female patient, whose case was demonstrated in the Charité (*Berliner Klin. Woch.*, 1900, 51 and 52) in November 1900. The lesions affected the chest and abdomen, as also the adjacent portion of the arms, and assumed the form of a large number of brownish-red tumours, the size of a lentil, which, as also the cysts present in them, clearly originated in the sweat glands, as is evident from an inspection of the figure. They may be classified as nævi tardivi, and more particularly as the variety of organnævi which are known as sweat gland nævi.

But in individual cases it was not easy to prove that the lesion was concerned with cysts originating in the sweat glands. In the specimen illustrated by the figure, this could only be rendered evident by the employment of high microscopic power. But then a characteristic feature is recognisable: the double stratification of the epithelium which follows the sweat gland type. Pick (*Virch. Arch.* 175) has rightly laid great stress upon the definition of sweat gland adenoma. Under a higher power it will be observed that a layer of mononuclear spindle cells is imposed upon the inner layer of cylinder epithelium. A colloidal mass is seen to occupy the interior of the cysts themselves. But even under a low power mutual communication between these latter, through persistent remains of sweat ducts, is to be made out. With but slight magnification, the single layer of the cylinder epithelium of the individual sweat ducts is readily obvious, while when a higher power is made use of, the double layer of cubical epithelial cells is an indication of an excretory duct of the sweat glands. In both figures the muscular layer, situated immediately beneath the epithelium, is recognisable in the form of mononucleated spindle cells between the connective tissue sheath and the epithelium. It is worthy of remark that, up to the present time, no direct connection of the prolongation of sweat ducts with the protective cells of the epidermis has been discovered in any case. It must therefore be inferred that these have been destroyed through an inflammatory process during fœtal life. But the sweat glands continue to secrete, and, inasmuch as the secretion cannot be discharged externally, it is clear that cystic degeneration must ensue. At least this is the theory supported by Lebet (*Annales de Dermat. et de Syph.*, April, 1905) and Pinkus (*Verhdlg. d. Berl. Dermat. Gesell.*, 1903, 1904. S. 105, *Derm. Zeitschrift*, Band xi.), who in Granulosis rubra nasi detected the early stages of hydrocystoma, and there would seem to be much to be said in favour of this view. Yet it is surprising that in the corium no trace of a previous inflammatory process can be detected.

Akanthosis nigricans.



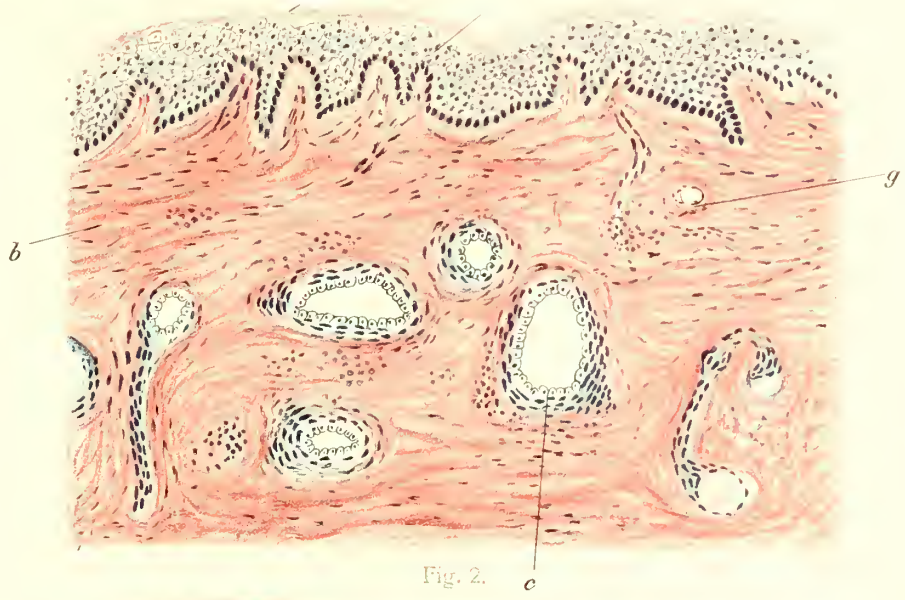


Fig. 2.

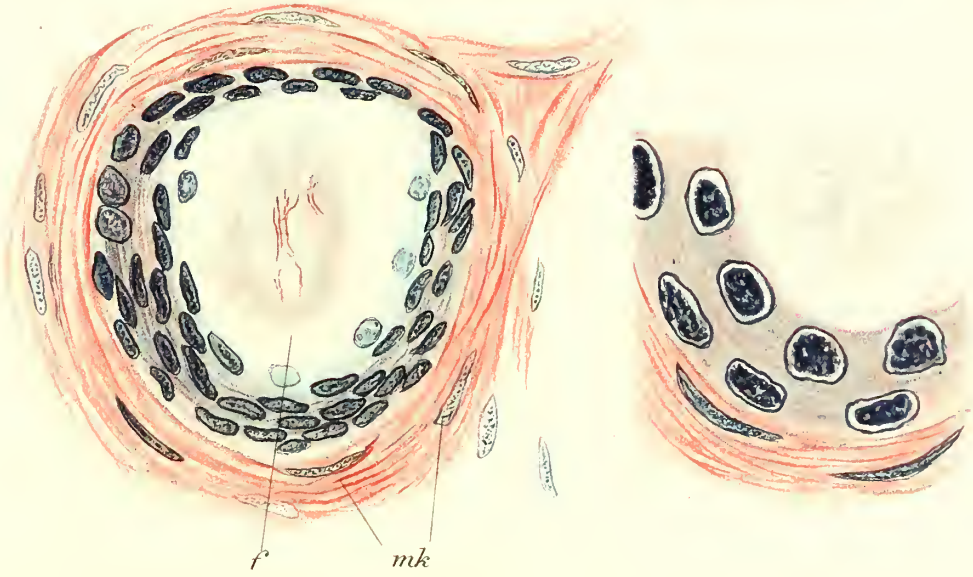


Fig. 3. Hidrocystoma tuberosum multiplex.

Plate II. Fig. 4. **Angiokeratoma.**

× 70, Obj. 3, Ocul. 2.

bl = blood, e = endothelium, s = sweat duct, p = nuclei, a = erythrocyte, strc = stratum corneum, r = rete, strg = stratum granulosum, b = connective tissue.

The figure includes an entire nodule of angiokeratoma. The epidermis is greatly elevated and falls away precipitously on both sides, the most marked prominence occupying the centre. The eminence is traversed by numerous corkscrew-shaped sweat ducts.

But the chief abnormality is observed in the papillary layer of the corium. The central vessels of the papillæ are very markedly dilated, and little by little a cavity is formed, the dilatation of which gives rise to the changes occurring both in the rete and the stratum corneum. Such cavities often render evident the communication with deep-seated blood-vessels which are markedly dilated, sometimes assuming an ampulla form.

The lacunæ remain for some time longer, surrounded by the tissue of the papillary layer, then they rapidly grow and manifest their characteristic tendency of penetrating between the layers of epidermis. They stretch the papillary layer, push forward the rete; in some places they break through the latter and press it against the resistant articulations of the epidermis. In such cases the tissue of the papillary layer has quite disappeared, and the cavities, excepting their bases, are bounded by the smooth flattened cells of the stratum cylindricum. These results of compression are distributed over the whole rete; they are particularly well marked if an epidermic cone is compressed by a cavity-containing neighbouring papilla; in this case they appear as if rolled up into a narrow band.

The size of the cavities varies very considerably; small yet complete intra-papillary spaces up to very extended cavities, which lead to the upper layers of the integument, are met with. On cross section they present oval, elliptical, finger-shaped, circular, in short, the most varied forms. Their long diameter is usually at right angles to the cutaneous surface. The internal structure of the lacunæ also varies very considerably. In the majority of cases they are divided by partitions into many chambers, and some of these possess their own particular coverings. The cavities are partly empty, partly filled with blood corpuscles which are closely pressed together and greatly shrunken: these corpuscles may be deeply coloured. On the other hand, merely a granular detritus, the remains of these corpuscles, may be observed. The partitions are sometimes straight, sometimes bent, and consist of several series of somewhat closely approximated cells which are processes of the chief walls forming the relics of the stratum Malpighii. Some of the cavities are covered with thin membrane, the remains of the firmly compressed together basal membrane and stratum cylindricum.

Plate II. Fig. 5. **Acne urticata.**

× Leitz, Obj. 3, Ocul. 4.

bl = vesicle, r = rete, n = necrosis, f = fibrin, ft = fat, t = sebaceous gland, m = musculus arrector pili, m = mast cells, i = infiltration, h = hair, g = vessel, strc = stratum corneum, s = sweat glands.

The preparation from which the section was cut was taken from a case of the disease attending my Polyclinic, which was carefully detailed by my deceased friend Löwenbach in the year 1899 (*Arch. f. Dermatol. und Syph.*, Band 49). We found at the extreme periphery of the primary eruption a simple but intense œdema of the cutis vera. In the papillary layer this œdema was so marked as to lead to an effusion of fluid in the apices of the papillæ; in this way very minute sub-epidermic vesicles were formed. The more nearly we approach the central portion of the primary eruption, the more clear does it become that this consists of a homogeneous necrotic mass with indefinite boundaries located between the epidermis and the papillary layer. This mass is traversed by fibrinous threads and is infiltrated with leucocytes. The middle of this necrosed area is penetrated by the duct of a sebaceous gland, of which the glandular structure and the associated hair follicle are surrounded in the cutis with a marked infiltration in which polynuclear leucocytes take a prominent part. It is clear that we have here a process of coagulation necrosis around a very pronounced croupous inflammation which involves both epidermis and papillary layer, and which is sharply separated from the surrounding tissues, as from those lying beneath. Acne urticata is distinguished from acne varioloformis by the location of the primary changes, infiltration, and œdema, in the peri-follicular cutis; the follicle itself, so far as regards its essential structure, remaining intact.

Fig. 4. Angiokeratom.

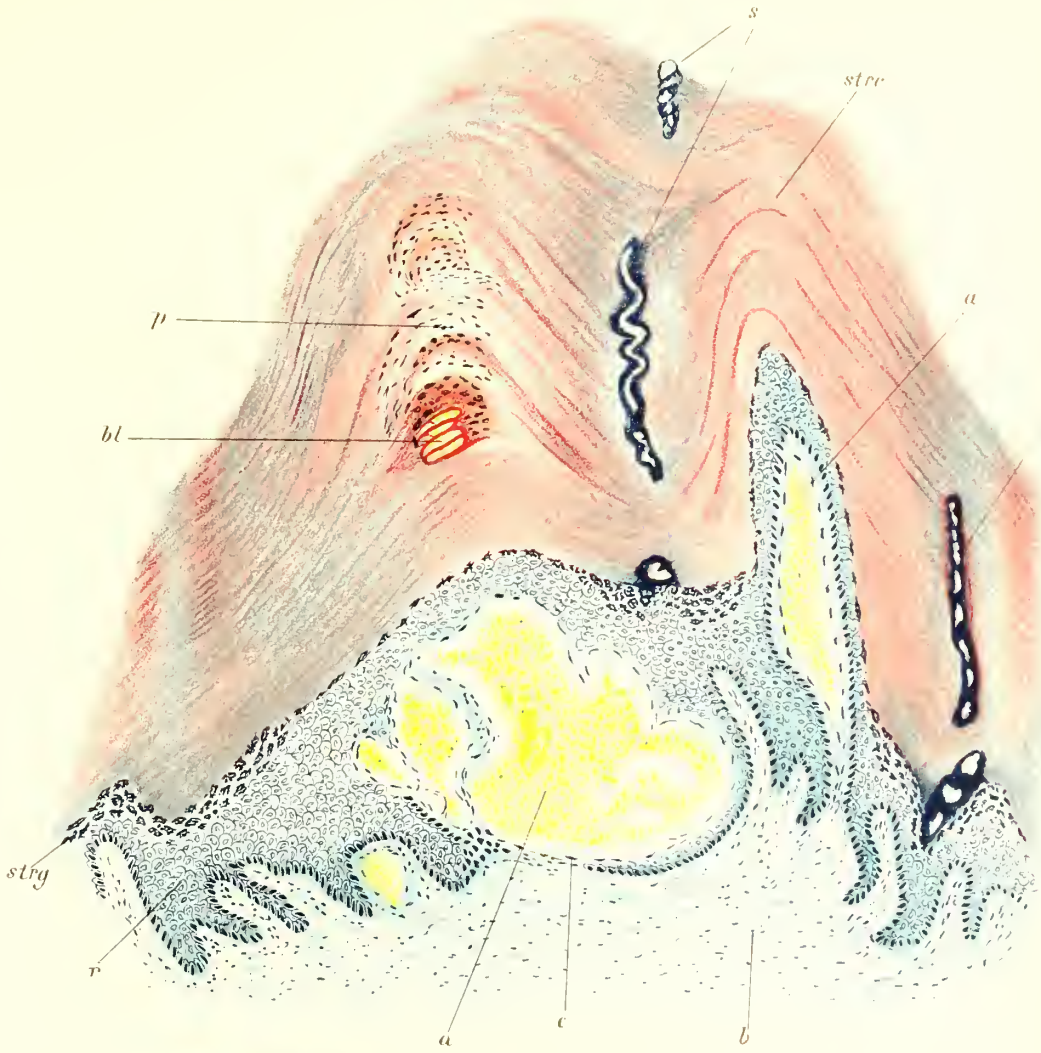


Fig. 5. Acne urticata.

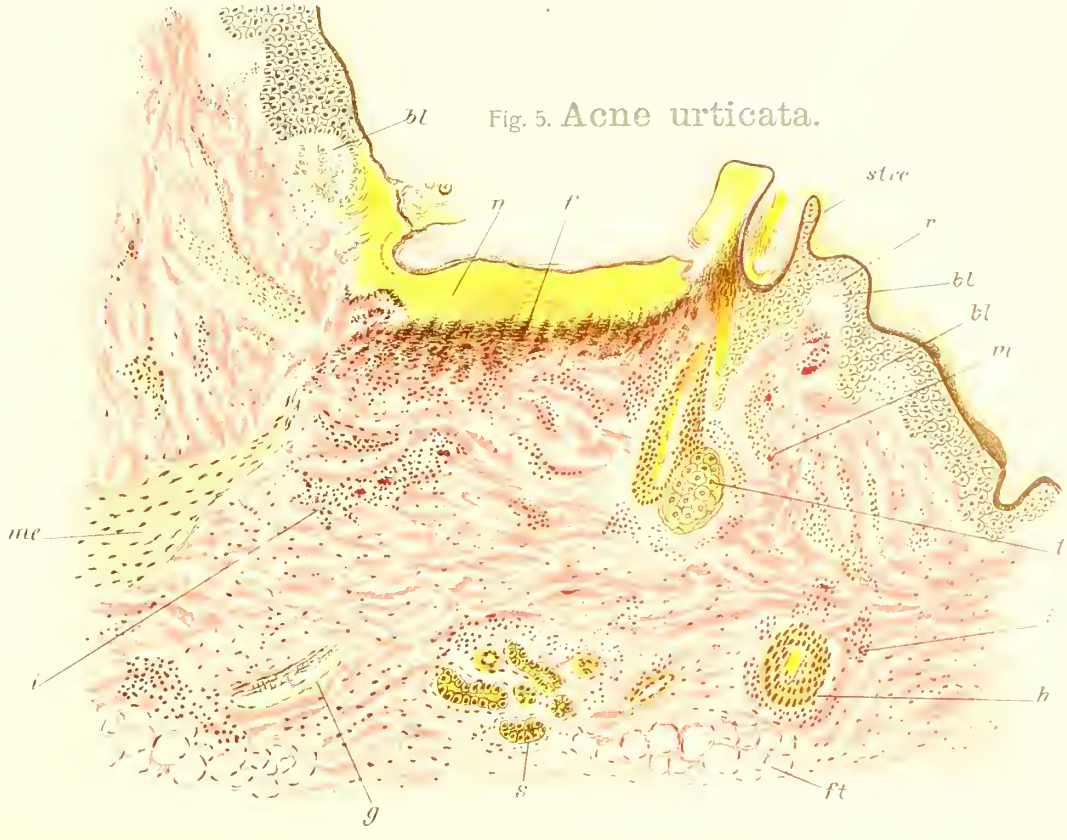


Plate III. Fig. 6. **Atrophia cutis progressiva.**

× 85 Leitz, Obj. 3, Ocul. 3.

e = old torn elastic fibres, f = newly formed elastic fibres, r = rete, h = hair, b = connective tissue, strc = stratum corneum.

It is a striking fact as regards scleroderma that both in it and in atrophy of the skin a marked thinning of the whole epidermis, as well as an atrophy of the papillary layer, is present. An essential distinction, however, exists, as concerns the behaviour of the elastic fibres. These are almost completely destroyed, and their presence can only be detected by the staining with orcein of the small quantity of broken-up remains of these fibres. These soft broken-up threads are scattered in an irregular manner throughout the preparation, and possibly in a longer or shorter time the remaining fragments will also disappear.

While in scleroderma the cells of the stratum corneum and of the rete are fairly well preserved, in Atrophia cutis propria these structures, as well as the papillary layer, become atrophied and take the stain badly. These changes affect only the superficial portion of the corium. The more deeply into the skin the investigation is carried, the more does the histological picture change its aspect, and here once more we find a large mass of thick, compact, dark violet-stained elastic threads apparently approaching the normal condition.

Inflammatory changes are completely absent, for the original abnormal process has run its course, and nothing more than the resulting atrophy remains.

The preparation is taken from a man of 36, in whom the atrophy was limited to the back of the hands and the forearms. The skin had a livid discoloured appearance, and to the touch gave the impression of crumpled cigarette paper. The veins could be clearly seen glimmering through the atrophied skin. It is possible that this is the terminal stage of a process which, according to Ehrmann, at its maximum is due to a chronic lymphangitis, and which terminates in degeneration both of the elastic and colloid tissue.

Plate III. Fig. 7. **Argyria localis.**

× 480 Leitz, Obj. 6, Ocul. 4.

c = capillaries, e = horny elastic fibres stained black through deposit of silver, i = infiltration, r = rete, strc = stratum corneum, strgr = stratum granulosum.

The preparation is taken from a worker in silver. Very fine detached particles of silver penetrate the finger during working hours; they become oxydised and affect only the elastic fibres. Hence, not only the coarse, but also the finest threads are stained right up to the neighbourhood of the rete. On the other hand, the rete and the stratum granulosum, as also the epidermis, are quite normal. Further, the corium presents no trace of inflammatory reaction. It is also obvious that the dark coloration depends upon the deposit of most

minute particles of silver. There is no complete diffused, dark staining of the elastic fibres, but under a higher power a granule lies alongside the others, staining the whole collection of fibres black. In the figure this is to be seen in some parts only. It is particularly interesting to find that the membrana elastica of the smallest capillaries is stained black.

The opinion of Liebreich that silver is oxydised in the tissues, and that the resulting oxide of silver is dissolved in the alkaline tissue juice and is then further reduced in the tissues, being deposited upon the elastic substance, is thus very probably correct.

Plate III. Fig. 8. **Angioma simplex.**

× 85 Leitz, Obj. 3, Ocul. 3.

strc = stratum corneum, r = rete, g = vessels, b = connective tissue, i = infiltration.

The figure represents a telangiectasis. This lesion is essentially composed of new formed vessels, and of vessels having newly formed elements in their wall.

The chief characteristic of a telangiectasis is the presence of numerous intercommunicating meshes, which at the periphery are bounded by clearly defined endothelium. As Virchow has pointed out, there is here a lesion consisting of a hyperplasia of capillaries forming a convoluted mass resembling the coils of the intestine. But the newly formed vessels do not consist merely of capillaries, for small arteries with thick walls of numerous layers are also met with. Hence it is often possible to feel a marked pulsation. Along with the telangiectatic development, there often occurs an abundant formation of cutaneous glands, of hair follicles, of musculi arrectores pilorum, and of fatty growth. Virchow attributes the tendency to swelling occasionally observed of these telangiectatic growths to the pronounced development of the musculi arrectores pilorum. By the contraction of these muscles the size of the tumour is reduced, and their relaxation produces a flaccid condition which may lead to subsequent swelling.

The opinion of Unna that Angioma is a wholly inelastic tumour would seem to be correct, as also his discovery that in Angioma the mast cells are the largest known.

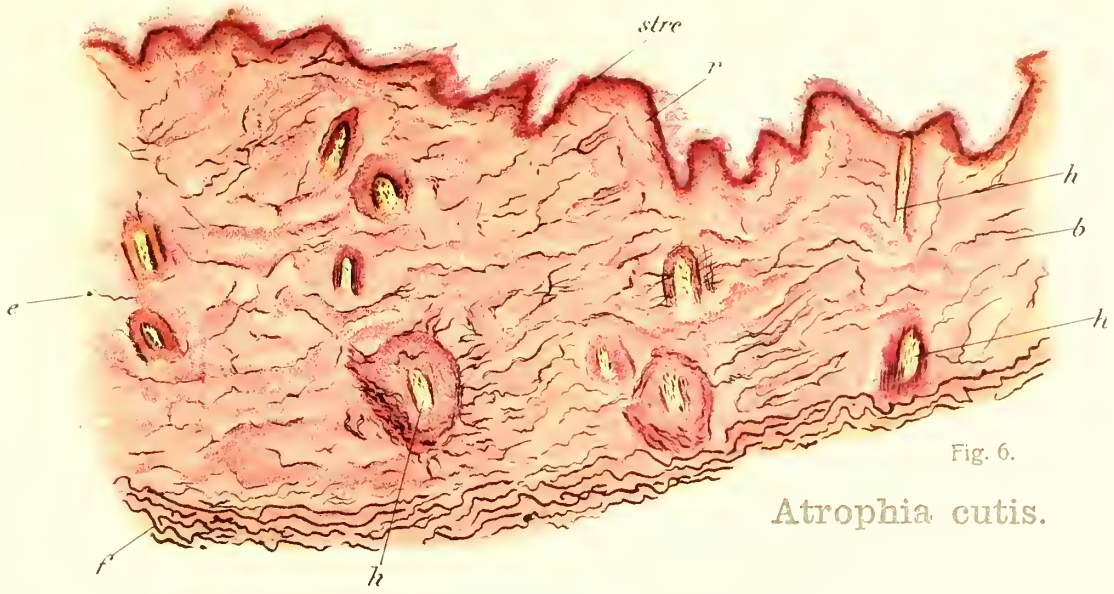


Fig. 6.

Atrophia cutis.

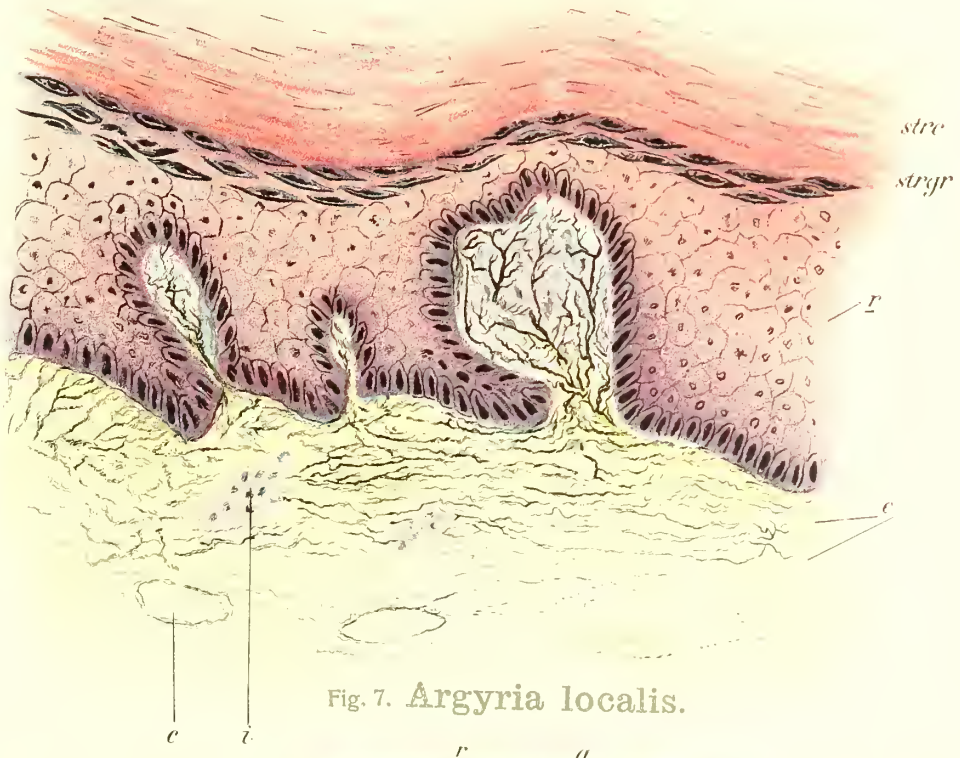


Fig. 7. Argyria localis.

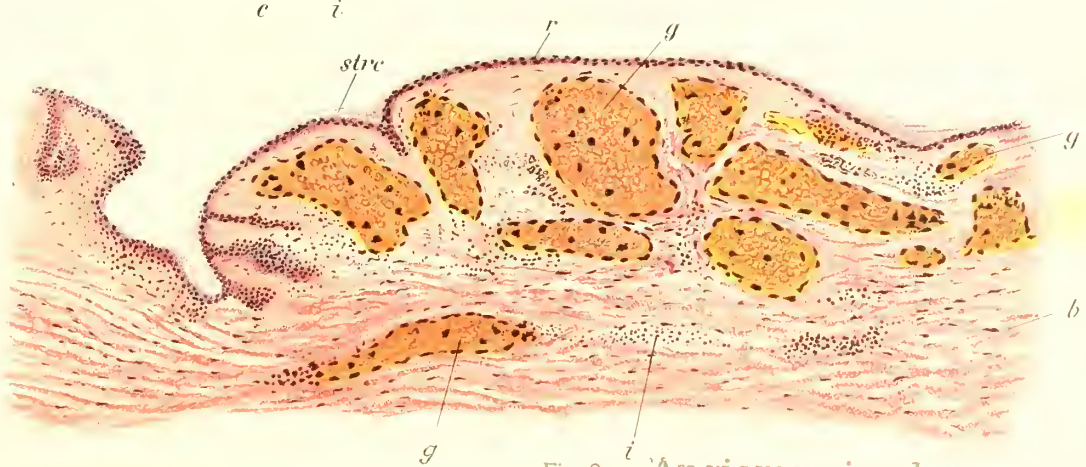


Fig. 8. Angioma simplex.

Plate IV. Fig 9. **Carcinoma primarium.**

× 105, Obj. 3, Ocul. 4, magnified 1000, oil immersion $\frac{1}{12}$, Ocul. 4, the follicle is represented sideways on account of restriction of space.

ca = carcinoma cells, k = kariokinesis, l = lymph, en = endothelium, p = papilla, e = epithelial cell, pl = plasma cell, g = vessel, b = connective tissue, i = infiltration, m = mast cell, r = rete, strc = stratum corneum, strg = stratum granulosum.

The figure represents a typical primary carcinoma of the skin. In this atypical overgrowth of the epithelium the connective tissue is penetrated by the epithelial cells. The several epithelial aggregations, arranged in alveoli, advance in solid phalanx against the more yielding corium. As evidence of the pronounced tendency to cell proliferation may be noticed the marked production of kariokinetic figures which is in progress; the mitosis is particularly pronounced at the periphery of the carcinomatous nests. Noticeable also is the asymmetrical division of cells in epithelial cancer, as observed by von Hansemann. In addition to the recognised forms of double, triple, and multiple division, he also noticed asymmetrical shapes, giving rise to irregular groups of loops formed of threads as the result of the formation of kariokinetic figures. Sometimes he noticed five and, again, nine loops, and in yet another instance the proportion was from eleven to sixteen. As a rule division into equal halves takes place, and von Hansemann could only regard this striking deviation from it as being by no means devoid of significance. The large fragments formed regular cells which at a later stage divided like their typical predecessors. Further, as inferred by von Hansemann from the presence of abundant nuclei made up of but few loops, and which contain but little chromatin, the smaller elements may form cells, and it is possible that these may divide to a certain extent in a normal manner. But, according to von Hansemann, the very various elements are ejected from the cells, and thereby continue to be more developed, more independent, and capable of propagation, forming exuberant cells with large nuclei and displaying kariokinesis.

These cancer cells lie closely compressed together and between them, contrary to what occurs in Sarcoma, no trace of intercellular substance can be detected. In this way the extremely rapid, indeed almost hurricane-like, progressive advance of cancer is explicable. Vessels are formed only in the stroma between the individual collections of cells; they are never present in the closed alveolar structures themselves. The epithelial cells show no fibrillation of their protoplasm, and between the epithelial nests are merely found some giant cells with their blue central nuclei and violet granulations, as also plasma cells with their eccentric nucleus and blue granulations. Eosinophiles are scarcely recognisable.

But both giant and plasma cells are numerically inferior to the leucocytes which infiltrate the tissue: this increase in the number of leucocytes must be regarded as a reaction on the part of the connective tissue against the penetration of the epithelial cell masses. The carcinoma cell masses act as foreign bodies,

and in this way give rise to a secondary inflammatory reaction with extravasation of leucocytes. From this point of view the path taken by the cancer cells in their further progress would seem to be most suggestive. Almost the whole of the lymph spaces of the upper portion of the corium are completely plugged with these cells, and hence it is no matter for surprise that dissemination by the lymph channels ensues with resulting metastasis.

Plate IV. Fig. 10. **Folliculitis.**

× Leitz, Obj. 3, Ocul. 3.

g = vessel, i = infiltration, strc = stratum corneum, strg = stratum granulosum, r = rete, m = mast cells, f = fatty tissue, p = plasma cells, sch = sweat glands, mc = micrococci, ch = chromatotaxis. The two last are × 800 Leitz, Obj. $\frac{1}{12}$ oil immersion, and Ocul. 3.

The original was taken from a girl whose forearm was the seat of an abundant, nearly symmetrical, and typical eruption.

The most important morbid changes occur in the sub-cuticular and fatty layers. In these localities pronounced inflammatory changes are observed in the adventitia of the vessels, especially of the veins. While the intima and media are merely the seat of slight thickening, or are to a large extent normal, in the adventitia an extremely marked infiltration of leucocytes is present: the infiltration consists chiefly of polynuclear forms, mononuclear cells being present in small proportion only. Interspersed are a large number of mast cells. The infiltration is more particularly discernible around the *vasa vasorum;* in this locality, indeed, a well-marked periphlebitis is present.

It is noticeable that this infiltration leads to the gradual obliteration of the vessels around which the inflammatory process has taken its rise; so marked is this occlusion that it is difficult to discover the existence of a lumen as regards these vessels. Hence it is not surprising that the papule is destroyed and that, as a result of the process of papule formation, an ultimate condition of papule destruction ensues.

The path followed by the assumed tubercular toxin in this disease is probably rendered evident by an infiltration of leucocytes which can be traced along the vessels up to the papillary layer. Along the lymph spaces situated on the route, and when these spaces are well formed and capacious, also around the sweat ducts, this effusion of leucocytes can be traced trending upwards to the epidermis, to the upper layer of which it attains. In the upper strata of the corium, and especially in the papillary layer, a noticeable infiltration is also evident, consisting of mono- and polynuclear leucocytes and giant cells.

In the vicinity of this infiltration in the fatty tissue numerous staphylococci are observed: these are probably secondary and have gained access through the ulcerated superficial patch: they have followed the pre-formed lymph passages in order to reach the deeper portions of the skin.

Fig. 9.

Carcinoma primarium.

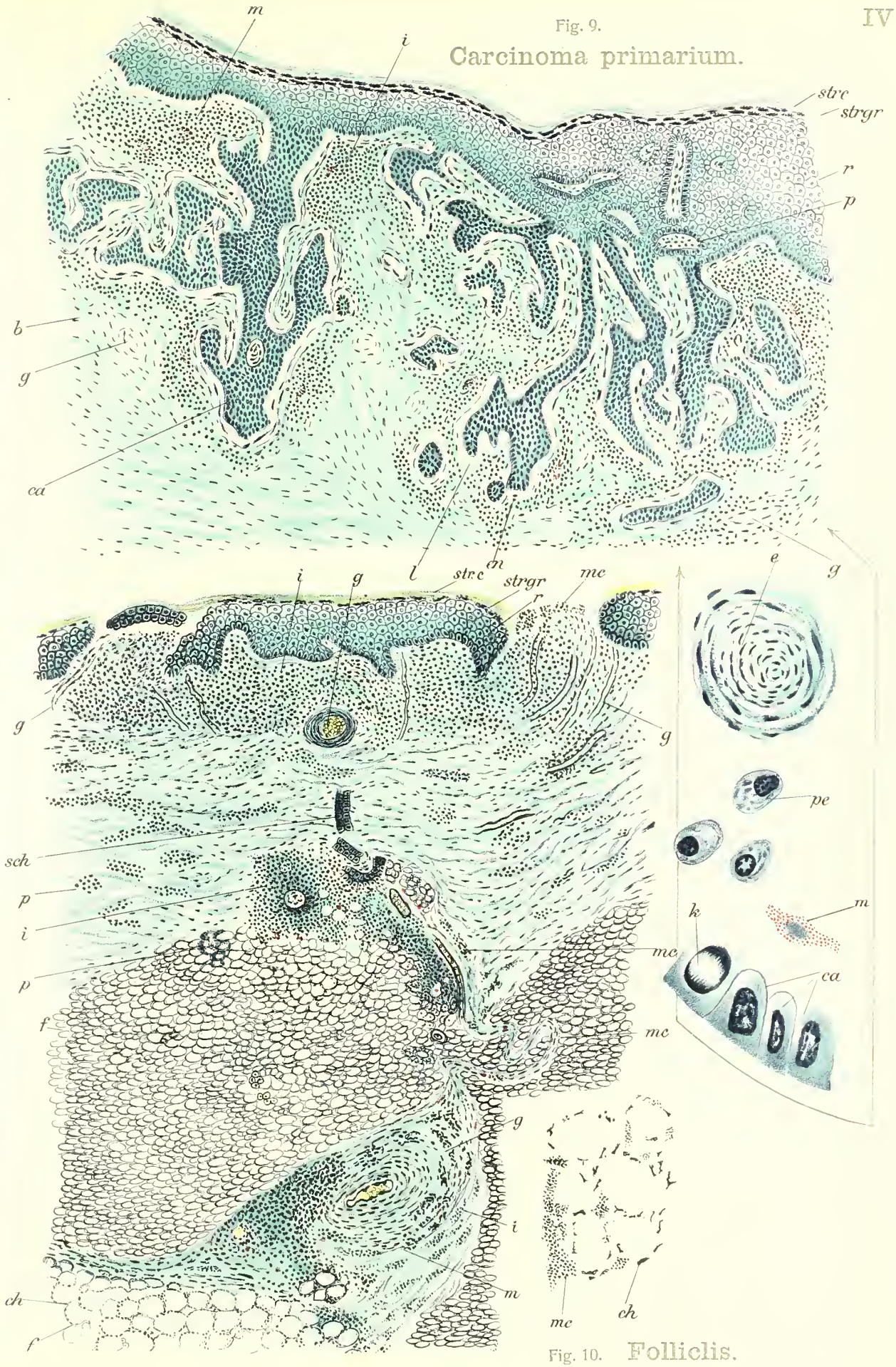


Fig. 10. Folliclis.

Plate V. Fig. 11. **Carcinoma Secundarium.**

× 85, Obj. 3, Ocul. 3.

a = artery, e = epithelial cells, b = connective tissue, l = lymphatics, filled with epithelial cells, strc = stratum corneum, r = rete.

Unlike the form of cancer described above, secondary cancer of the skin is extremely rarely met with. The case from which the figure is taken was that of a man of 48 suffering from primary cancer of the bladder. Shortly before death a large number of localised sharply defined nodules appeared in the skin occupying the most varied situations and apparently seated deep down in the substance of the corium.

On microscopical examination it was at once obvious that a large number of the lymphatics occupying the upper layer of the corium was stuffed with typical epithelial cells. Metastases arising from the bladder lesion had developed, and these had attacked the skin, assuming the form of an embolic infarction of the cutaneous lymphatics. It is clear that the cells in the latter must be of the same type as those of the bladder.

Plate V. Fig. 12. **Lepra tuberosa.**

× 370, Obj. 7, Ocul. 1 and × 1000, oil immersion $\frac{1}{12}$, Ocul. 4.

l = lepraglobi, lb = lepra bacilli, lc = lepra cells, k = nucleus, v = vacuole, b = connective tissue, c = connective tissue nucleus, r = rete, str = stratum corneum, strg = stratum granulosum.

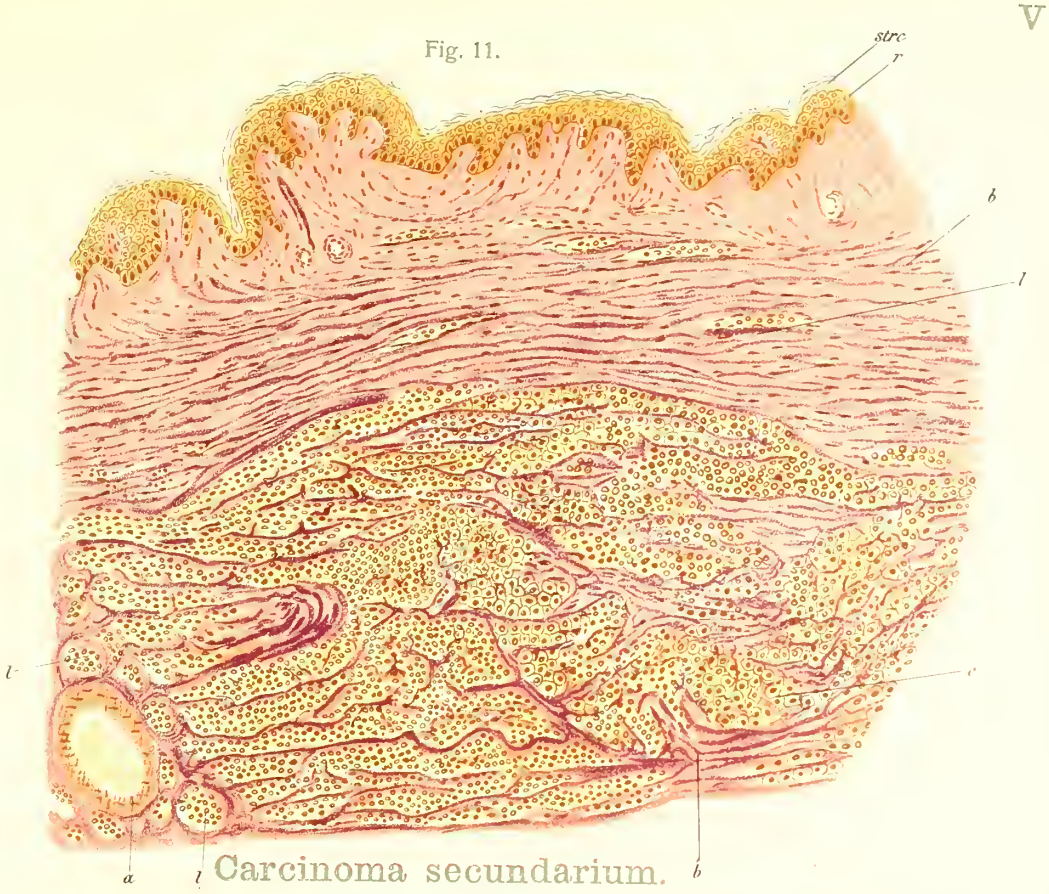
The histological aspect of lepra reverts completely to the bacillary invasion. In a specimen which has been successfully stained with carbol-fuchsine, methylene blue being employed as counter stain, the red bacillary aggregations are observed to contrast well with the blue background. The rete, stratum granulosum, and stratum corneum display but little acanthosis and hyperkeratosis. Further, the upper portion of the corium remains tolerably free from bacilli, and it is only in the middle and lower portions of the corium in a well-marked case of Lepra tuberosa, such as the one here depicted from Brazil, that the bacilli are found in thousands, either isolated or in aggregations, some lying free in the connective tissue, while others are distributed in the lymphatics. The bacilli assume the characteristic cigar bundle arrangement, and present the superficial appearance which Virchow described as characteristic of lepra bacilli.

The lepra cells are recognisable by their size, and possess one or more nuclei and a remarkably altered protoplasm in which one or several unstained vacuoles

are present. In these cells the bacilli are but seldom to be observed in the protoplasm and between the vacuoles. The proof that we have here under observation, not sections of vessels, as maintained by Unna, but cells, lies in the fact that occasionally, through the formation of vacuoles, the nucleus may be detected, forced, as it were, towards the periphery of the cell. Further, the lepra bacilli are met with not only in the lepra cells, some of which take origin in leucocytes, others in connective tissue cells, but also sometimes lying free in the lymphatics.

The anatomical sub-stratum of the leprosy new formation consists of granulation tissue which is in the first instance developed in the corium in union with the vessels, but which is invariably separated from the epidermis by a layer of healthy connective tissue. The infiltration presents itself either in the form of circumscribed nodules, or else is widely diffused. Round cells are mostly present, the spindle forms being few in number. Within the leproma the elastic fibres are completely destroyed. Typical giant cells are occasionally observed. As a result of the extremely chronic progress of the disease, only slight evidence of retrograde metamorphosis can be detected, and to this retrograde process appertain the " gelben Schollen " (Hansen) or " Globi " (Neisser) which are the results of the degeneration of nuclei and of cells.

Fig. 11.



Carcinoma secundarium.

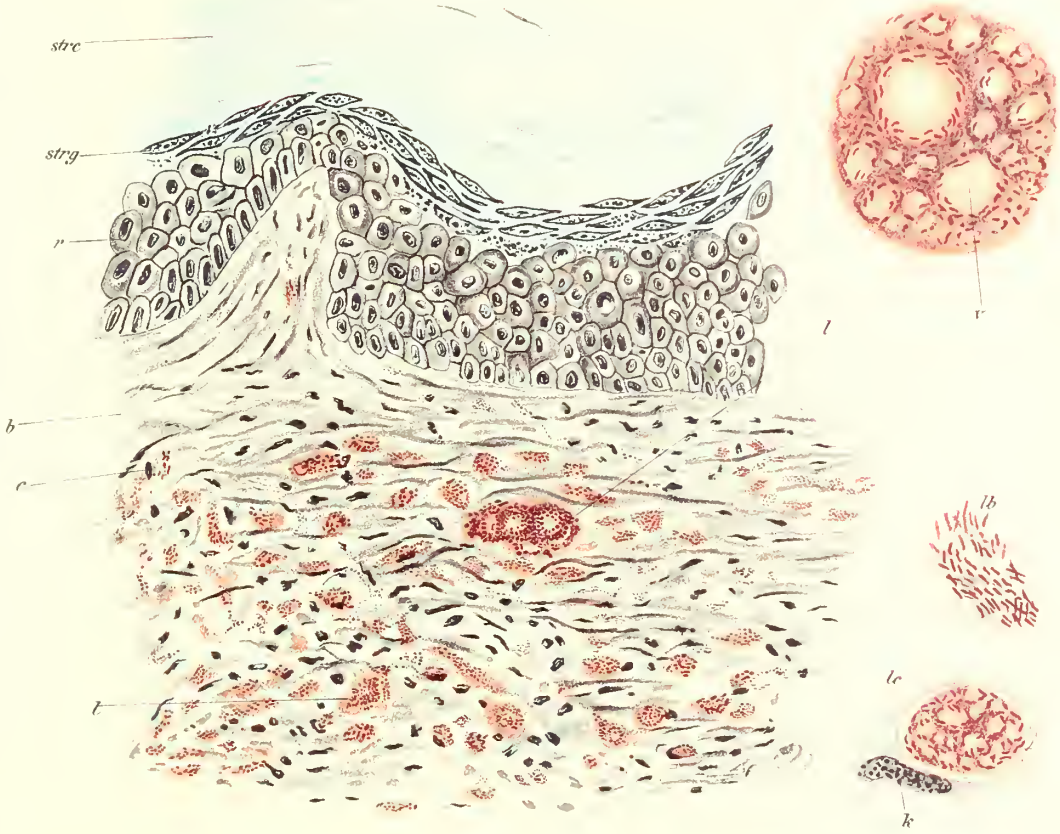


Fig. 12. Lepra tuberosa.

Plate VI. Fig. 13, 14. **Erythema exudativum multiforme.**

× 105, Obj. 3, Ocul. 4, × 1000, Oil immersion $\frac{1}{12}$, Ocul. 4.

d = degenerate rete cells, bl = vesicle, g = vessel, c = micrococci, r = rete, strc = stratum corneum, strg = stratum granulosum.

It is perhaps possible to recognise the antecedent exudation as being the result of the primary supposed toxin which sets up a serous exudation accompanied with a moderate inflammation in the corium. In comparison with other forms of primary dermatitis of a genuine inflammatory character, this variety is very trivial, but nevertheless the capillaries are seen to be markedly dilated, and around them is observed an infiltration of mononuclear and a few polynuclear leucocytes, which in certain definite localities, and more especially around the sweat glands, is very pronounced. The exudation gradually becomes so marked that this formation of vacuoles (described by Unna as "ballooning") by degeneration of rete cells ("altération cavitaire"—Leloir) grows yet more pronounced, so that through intra- and sub-epithelial manufacture of minute vesicles, as also through flattening of the rete cells, a genuine vesicle formation between rete and corium takes place. Then a diffuse œdematous saturation of the upper portion of the corium ensues, and, acting to some extent as supporting pillars, the papillæ divide the vesicles into different compartments. The papillæ resemble the pillars of a bridge, whilst all around them the exudation has completely flooded the river bed.

But in process of time, as is shown in the figure, the rete cells undergo necrosis, as does also a portion of the superficial epithelium; within the vesicles the necrosed epithelial cells may be observed to float. Occasionally, when a higher power is made use of, a number of ordinary cocci, chiefly streptococci, are discernible, and in the upper portion of the corium, more especially limited to the papillary layer, a pronounced inflammatory infiltration is present. The latter is chiefly made up of a proliferation of fixed connective tissue cells, between which the dilated capillaries are seen to pass along in palisade form. In the immediate proximity of the papillary layer this inflammatory process abruptly ceases and gives place to normal conditions.

Plate VI. Fig. 15. **Favus herpetiformis.**

× 85, Obj. 3, Ocul. 3, and × 1000, Oil immersion $\frac{1}{12}$, Ocul. 3.

f = favus fungus, ms = muscul. arrector pili, r = rete, i = infiltration, t = sebaceous gland, h = hair, g = vessel, strc = stratum corneum, strgr = stratum granulosum.

The figure is drawn from the same original preparation as is the one depicted by the author and Meissner in the Atlas of Histopathology of the Skin, and rendered as a microphotograph in Plate XXIV. of the same work. Hence it was necessary to institute a comparison between a photograph and a coloured reproduction. Thus the description given in the Atlas may be repeated here.

At the orifice of a hair follicle there is seen, both under a low and a high power, an extraordinary entanglement of mycelium and spores of the *Achorion Schoenleinii*. The fungus growth forms a round hemispherical prominence which is surrounded at its edges by a narrow layer of horny cells. The fungus growth is bounded below by the upper layers of the rete Malpighii. The whole structure is known as a *scutulum*. Unna has very accurately observed a characteristic of the structure: the perpendicular protrusion of the mycelial threads from the epidermis.

The threads of mycelium form finely granular unstained masses; no nuclei or other remains of cells can be detected in them. The rete Malpighii, as also the outer and inner root sheath of the hair, displays no alteration. On the other hand, the hair itself is enveloped by the threads. Also in all the hair follicles shown in the figure fungus threads are discernible closely encompassing the hair. Mibelli's assertion that, in the course of examination of a very large number of favus preparations taken from different localities, and in which the hairs were well preserved, he had never been able to find a sebaceous gland, I am unable to substantiate. In the vicinity of the vessels, especially within the papillary and in the sub-papillary zone, many cells presenting the appearance of young connective tissue cells may be observed to have accumulated. The frequent occurrence of kariokinetic figures points to the autochthonous origin of these cells. The vessels themselves are not dilated; the capillaries are here extremely prolonged.

Mibelli correctly points out that under the scutulum an inflammatory process is in progress, and that this leukofibrinous exudation probably supplies the fungus growth with nutritive material. This inflammation is rendered evident through the tendency to superficial and follicular hyper-keratosis, and the consecutive atrophy due to the fungus growth, which ensues, is the natural consequence of the pressure which the scutula exert on the inflamed skin during long periods.

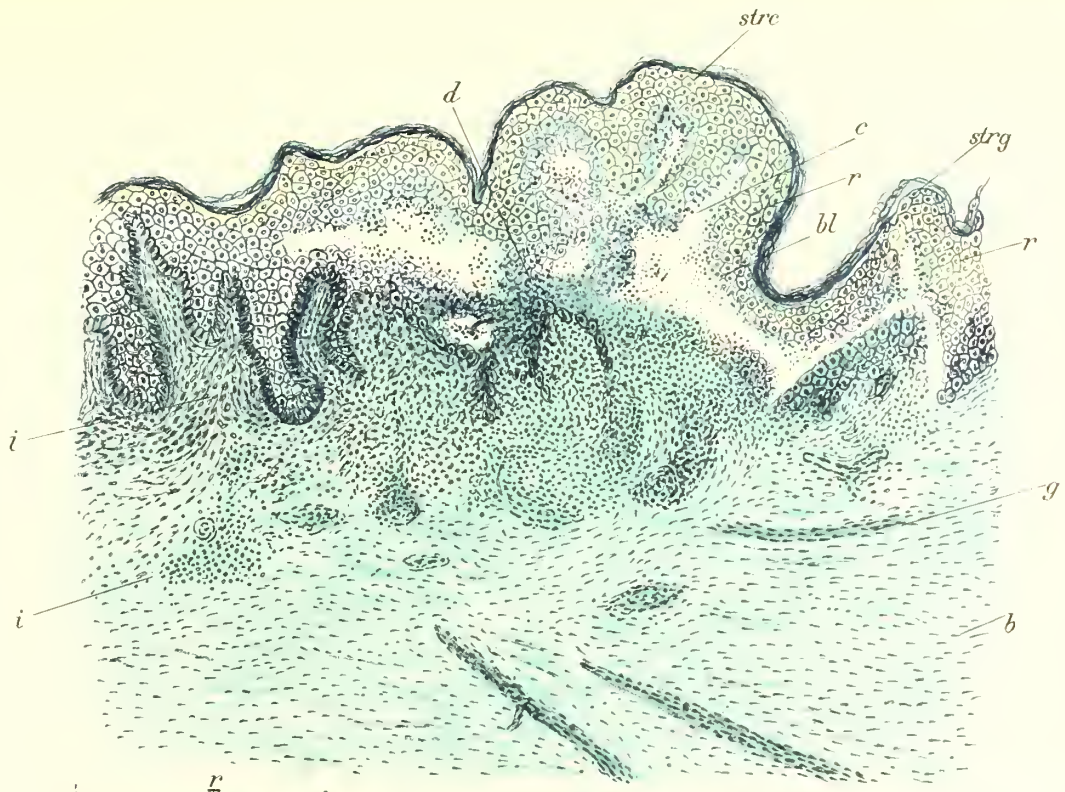
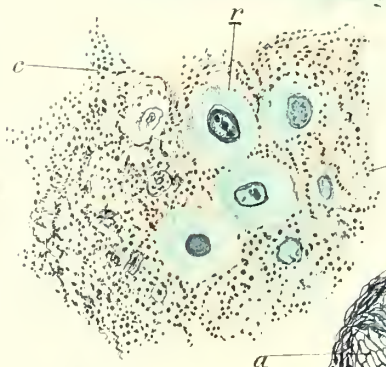


Fig. 13. Erythema exsudativum multiforme.



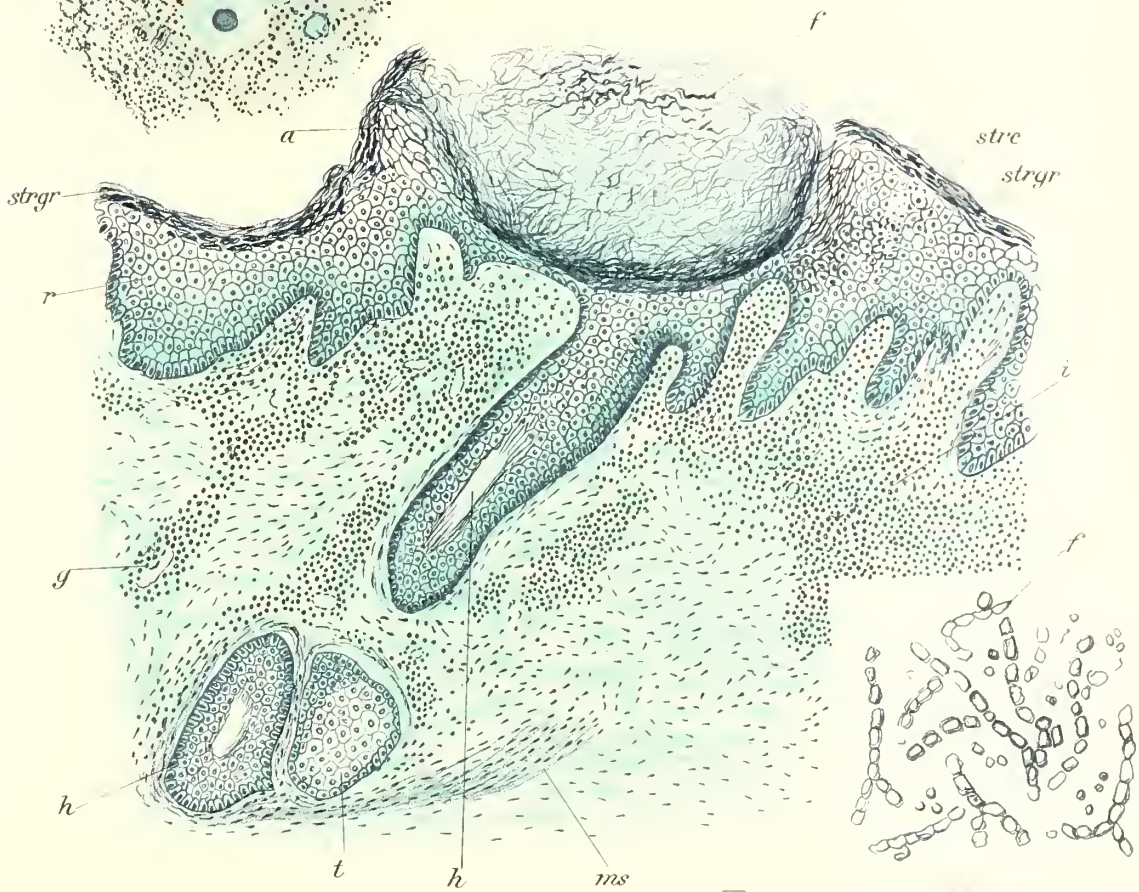


Fig. 15. Favus herpetiformis.

Plate VII. Fig. 16, 17. **Fibroneuroma.**

× 85, Obj. 3, Ocul. 3.

n = nerve, b = connective tissue, r = rete, strc = stratum corneum.
The axis-cylinder (a) and neurilemma (n) are × 528, Obj. 7, Ocul. 3.

I am tempted by the singularity of this case to afford it a place in the Atlas. In a man of 45 suffering from multiple mollusca fibroma (Recklinghausen's disease) a tumour was present, which was exceedingly painful, and when handled felt firmer than the ordinary sensitive, soft fibromata. I removed this sharply defined tumour, which was situated on the flexor aspect of the forearm; the growth was about the size of a pea and was extremely sensitive to the touch. When examined microscopically it proved to be made up of a multitude of myelinated nerve fibres which were very clearly defined by Van Gieson's stain in almost tumour-like arrangement. The epidermis and rete are normal, and the upper third of the corium is healthy, while in the middle and lower thirds of the same a large number of normal nerve fibres are observed both lengthwise (l) and cut at right angles (n), the axis cylinders of these fibres being very closely approximated. There is no trace of interstitial neuritis, or of inflammation of the connective tissue elements of the corium.

When magnified to 525 (Leitz, Obj. 7, Ocul. 3), the cross section of the nerve is seen to present no trace of inflammation as regards the nucleus or its vicinity. Hence it would seem that we have here a good example in favour of the view held by Von Recklinghausen, that a portion of the cutaneous fibromata ultimately displays the structure of neuromata of the skin.

Plate VII. Fig. 18. **Variola.**

× 85, Obj. 3, Ocul. 3.

g = vessels, strc = stratum corneum, b = connective tissue, bl = vesicle formation, f = fat, h = hair, c = micrococci, r = rete, f = fat cells.

In the immediate neighbourhood of a hair a large akantholytic many-chambered vesicle is seen. In these words the most comprehensive definition is expressed of what is implied, from the cutaneous point of view, when the term *variola* is made use of. It must, of course, be clearly understood that no general conclusion as to the pathology of variola is to be drawn from the histological study of the cutaneous phenomena of the disease. In all probability the formation of vesicles which occurs is the secondary phenomenon which can be studied on the skin, whilst the primary changes, due to the infective agent proceeding from the interior outwards to the cutaneous surface, are reproduced by photography.

Contrary to what obtains in the vesicles of herpes, the variolous pustule is furnished with a wide basis occupying the surface of the skin, and is sub-divided into several chambers by regular partitions. It is formed by the destruction of the deeper layers of the rete, with implication of the corium, while the epithelium above the vesicles forms a moderately thick dome-like covering to the same. The contents of the vesicle consist of abundant lymphocytes and of a large number of micrococci.

The mode of origin of the vesicle in the deeper portion of the rete, the œdematous soaking, and the destruction of the papillary layer all indicate that ultimately secondary scarring must ensue at the site of the variolous pustule.

The infiltration of the corium is less marked than in herpes zoster. But while in the latter malady the cell infiltration is not followed by any severe destruction of the connective tissue, and hence it is possible for restitution to take place at a later stage, in variola the corium is severely implicated. The connective tissue becomes the seat of swelling and of hyaline degeneration, is very œdematous and is beset with broken-down extravasated leucocytes, all these changes pointing to a severe intoxication of the cutaneous structures. It is therefore no matter for surprise that in these localities deeper scars develop than in herpes zoster.

At the commencement of the process the blood-vessels of the corium are greatly distended, and as regards the fully developed pustule, I can substantiate what Unna (*Histopathologie der Hautkrankheiten*, Berlin, 1894, S. 643) maintains, that in the adventitia of the blood vessels a marked accumulation of plasma cells occurs, while mast cells are present in small quantities only.

In variola there is met with, along with the ballooning degeneration, as already mentioned in connection with herpes zoster, the reticulated colliquation of the epithelium particularly described by Unna (*Unna's histol. Atlas zur Pathol. der Haut*, Hamburg, Voss, 1900, Heft 4, S. 95):—" This degeneration displays appearances diametrically opposed to those of ballooning degeneration. In reticulating degeneration intra-epithelial vessels are present which are separated by continuous walls, while ballooning degeneration gives rise to a liquid cell pulp which is found in a large inter-epithelial vesicle, inasmuch as the prickle shields of the epithelium contemporary with the cell wall and the plasma are melted down into a homogeneous fibrinous mass. But the nucleus maintains a wholly independent position. It slowly crumbles and diminishes in size without losing its colorability, but also without displaying a tendency to mitotic or amitotic division. There is never, as in ballooning degeneration, a formation of polynuclear and giant cells. As regards the prickle cells, as a rule the first formed, those of the cutis, approximate the ballooning, the later produced the reticulating type of colliquation. In variola when both forms of degeneration co-exist, the reticulated is confined to the upper prickle layer."

The so-called protozoa found in the variola pustule by Pfeiffer and others Unna correctly regards, and particularly on account of their cystic form, as being identical with his ballooned epithelial tissue. He maintains that, as a result of fibrinous metamorphosis, cystoid forms may be produced from epithelial cells.

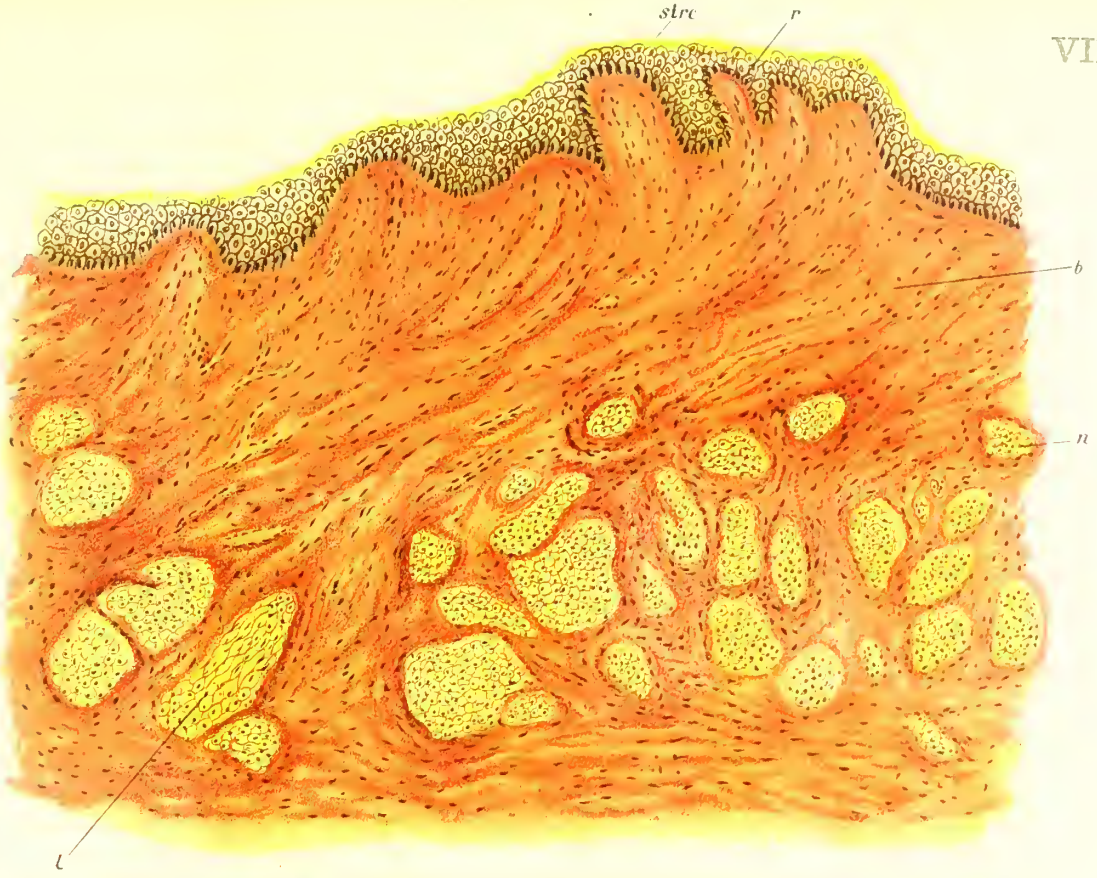
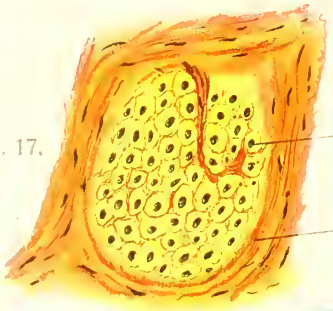


Fig. 16. Neurofibroma.

Fig. 17.



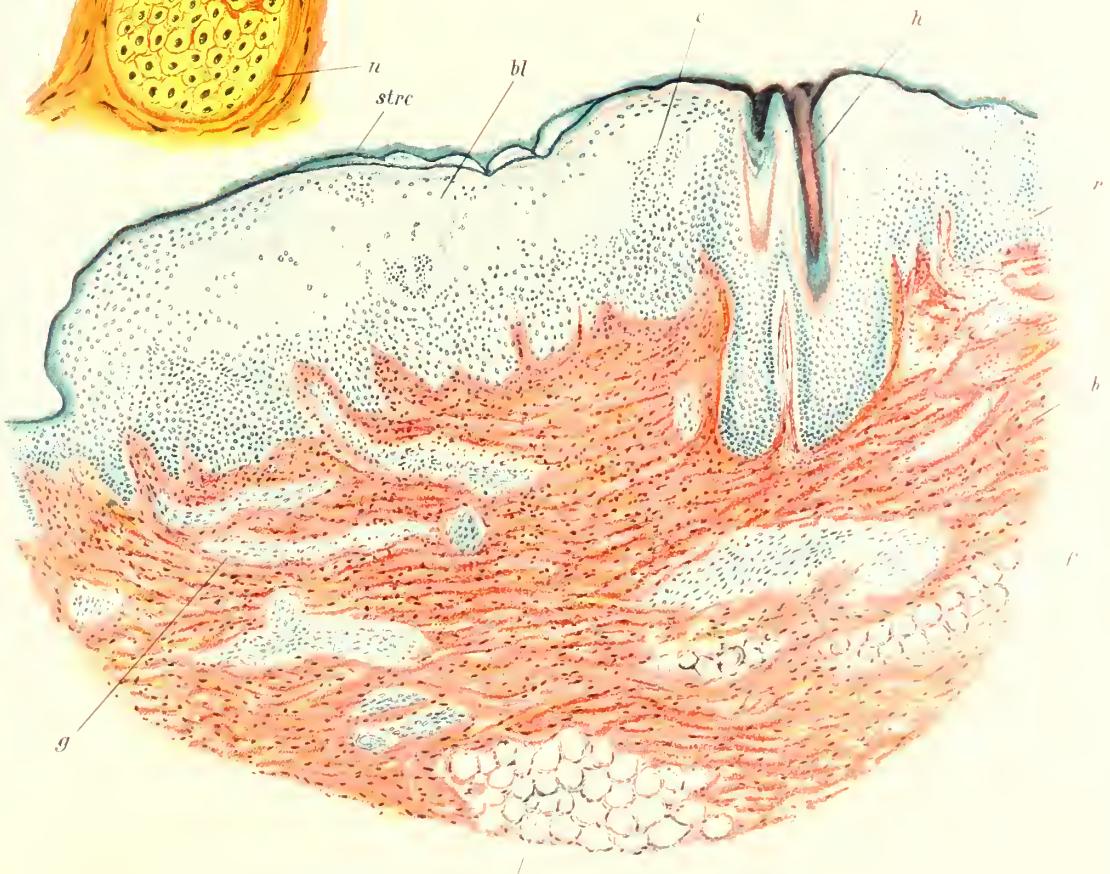


Fig. 18. Variola.

Plate VIII. Fig. 19. **Glossitis gummosa.**

× 70, Obj. 3, Ocul. 2.

ka = chromatotoxis, ri = giant cells, b = connective tissue, ms = muscle, r = rete, g = vessel.

In the first portion of the Atlas of Micro-pathology, produced in collaboration with Meissner, a representation of gumma of the skin is given in Plate XIX., fig. 38. Supplementary to this I here present a figure of a gumma of the mucous membrane of the tongue.

It is at once observed that the gumma has taken origin in the musculature of the tongue, and has then encroached on all the structures right up to the surface of the organ, including these structures in a uniform destruction. At the surface the hypertrophied epithelium and the widened and lengthened tongue papillæ offer a resistance to the further progress of the new growth. But in other localities the epithelium is itself already involved in the disease, and the original tissue is almost entirely destroyed, in spite of the presence of many mononuclear and but few polynuclear leucocytes which are detectable in the vicinity of the vessels. Further, the loose consecutive tissue between the individual bundles of muscular fibres is already copiously infiltrated with cells in the depth of its structure. Within the new growth itself some few muscular fibres are still present, yet in these fibres, as is evident from the wavy sarcolemma which surrounds them like a loose bag, it may be safely assumed that the process of destruction has commenced. The giant cells stand out here in a remarkably prominent manner; they may be regarded as foreign body giant cells, and in my experience are not infrequently met with in cutaneous gummata as well as in those of the mucous membrane and the intestines.

In other localities, fatty degeneration of the thick granulation tissue has occurred, and the central portion of the gumma appears to be necrosed. Yet it must not be forgotten, as Baumgarten has pointed out (*Virch. Arch.* 97 Bd.), that the structural outlines of the caseous masses of syphilitic material vanish but slowly, and that vessels filled with blood corpuscles have remained for long periods within these caseous aggregations.

Plate VIII. Fig. 20. **Herpes Zoster.**

× 105, Obj. 3, Ocul. 4.

v = ballooning degeneration, bl = vesicle, rc = rete cells, s = cocci, strc = stratum corneum, r = rete, i = infiltration.

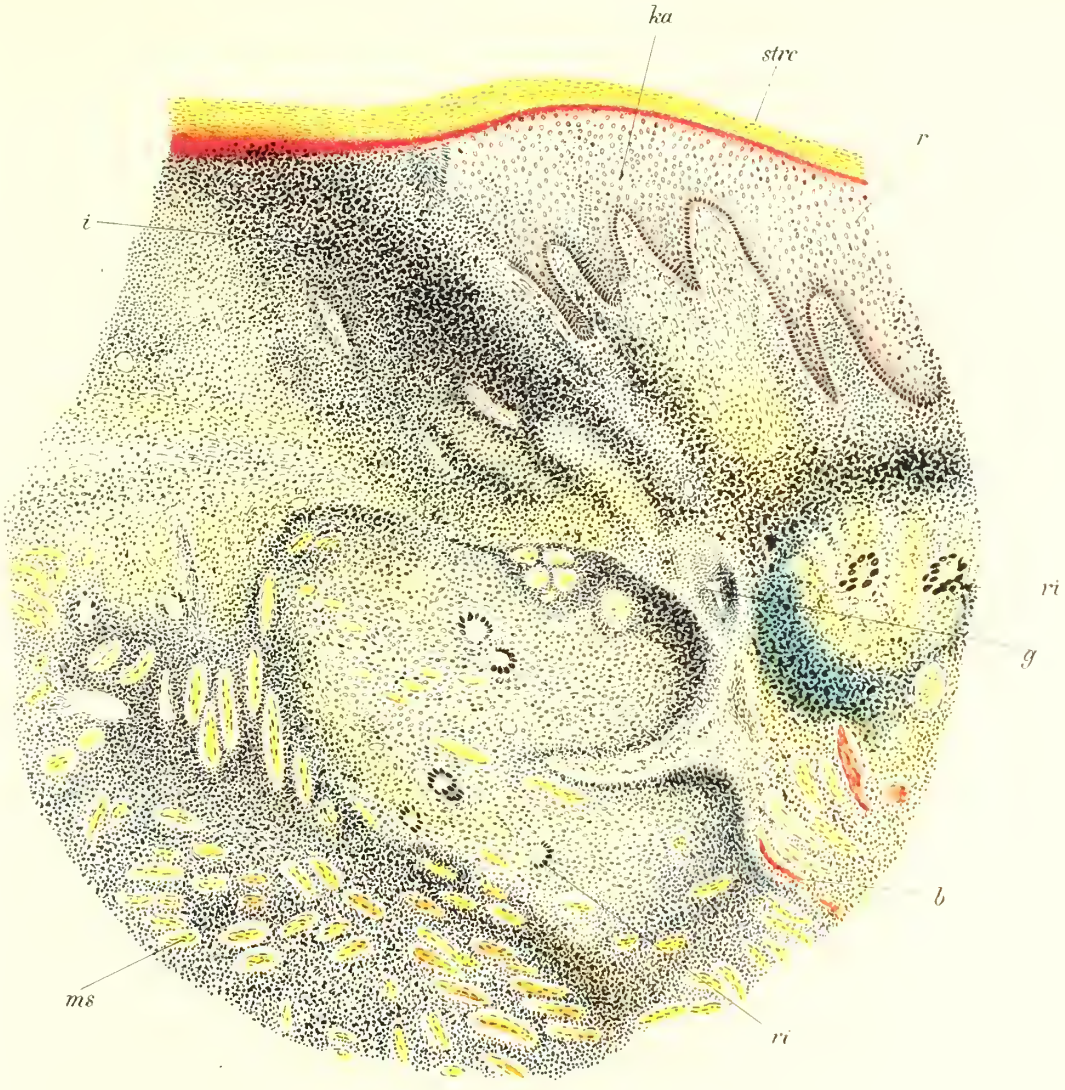
A semicircular vesicle projects from the rete, which it destroys, and is covered superficially with a thin but healthy stratum corneum. In the multilocular vesicle, in addition to sero-fibrinous effusion, a quantity of epithelium with

swollen contents, some leucocytes, and the usual cocci are present. Bethmann (*Münch. Med. Woch.*, 39, 1898) has occasionally detected many eosinophiles in the zoster vesicles, whilst according to Kreibich (*Die Angioneurotische Entzündung*, Vienna, 1905, S. 46) in every typical zoster the earliest stages are attended with exudation of eosinophiles, and later with that of neutrophiles. The cells of the stratum Malpighii are spread out so as to form both spindle and various other shapes, and the epidermis, together with the most superficial layers of the rete, is raised up so as to form a vesicle.

In this connection Unna calls attention to an alteration of the epithelial cells which he describes as being affected with "ballooning degeneration." According to his observation, the prickle cells become rounded off and the whole of the normal fringe of prickles of the cells destroyed. It would seem, to quote the simile of Unna, as if it were taken up into the cell mantle, much in the same way as a snail draws in its horns. At the same time the mutual union between the epithelial elements is dissolved, and the cells lie at the bottom of the vesicle, forming a heap of isolated fragments. According to Unna, this abolition of the mutual connection between the epithelial elements explains the tendency to the formation of monolocular vesicles. Subsequently an amitotic increase of nuclei ensues. There is, further, an inter-epithelial development of vesicles. Weigert regards the zoster vesicle as the type of a colliquative vesicle, in which the epithelium is already shed when the latter is saturated with the effusion.

A somewhat pronounced infiltration is present in the corium; it consists chiefly of mononuclear cells, and is especially abundant around the vessels. This infiltration is so much in evidence in the papillary layer that, in union with a serous exudation in the corium, it forces apart the connective tissue portion. In this way the nutritive supply of the connective tissue may be compromised and the tissue may necrose; and hence it is that after the occurrence of an attack of zoster scarring is sometimes left.

Fig. 19. Glossitis gummosa.



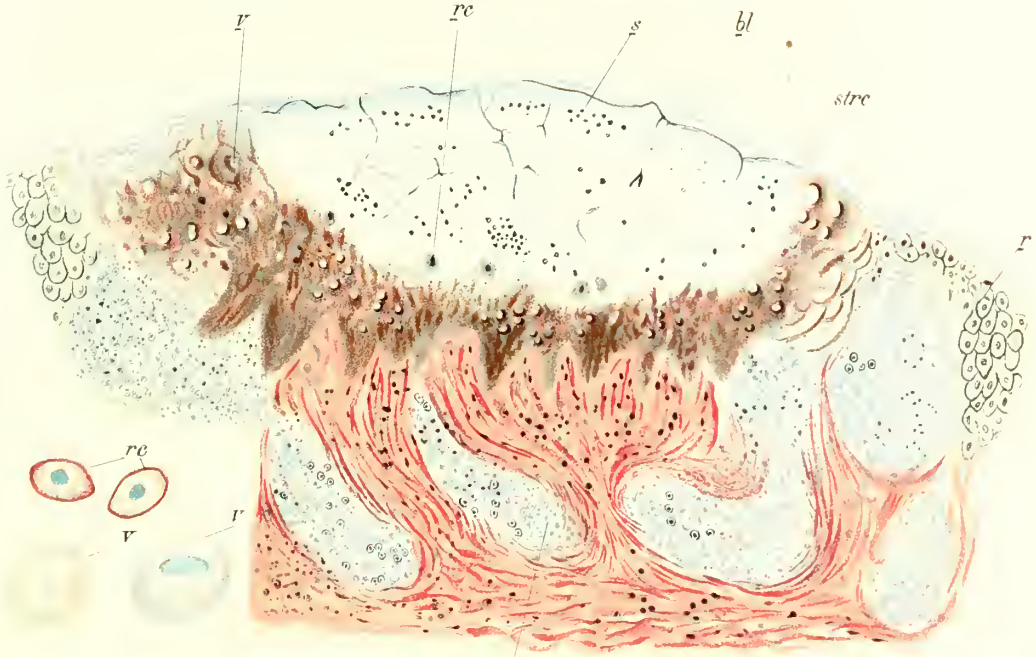


Fig. 20. Herpes Zoster.

Plate IX. Fig. 21. **Gonorrhœa chronica, soft infiltration.**

× 47, Obj. 2, Ocul. 3.

e = epithelium, mo = lacunæ Morgagni, l = glands of Littré, ac = desquamated epithelium, b = connective tissue, infiltration of leucocytes, g = vessels.

Near to the lacunæ Morgagni the glands of Littré project in a prominent manner. The flat depressions of the lacunæ (mo) are distinguished through their distension with cylinder epithelium arranged in several layers and which is in process of desquamation. As evidence of a chronic inflammatory process abundant overlapping nuclei are observed. Further, in the cavities formed by the lacunæ cast-off desquamated epithelium is collected, together with a few mononuclear leucocytes. By a happy chance the section has included a duct of a gland of Littré, and in this area is observed the same process of active cell proliferation as was evident in the lacunæ Morgagni. Here once more the cylinder cells alternate with mononuclear leucocytes. It is obvious that if gonococcii have once been deposited in the deeper portions of the glands of Littré it must be difficult to effect a *restitutio ad integrum*.

The third striking feature of this preparation is the sub-mucous cell infiltration, which is formed of a large collection of mononuclear leucocytes; these are interspersed with but few polynuclear leucocytes.

Hardly any mast cells can be detected; on the other hand there are large numbers of plasma cells furnished with eccentrically placed nuclei and granular protoplasm.

From the study of a preparation such as the present of soft infiltration in chronic gonorrhœa, the reason becomes clear why, in endoscopy, the openings of the glands of Littré, not evident in the normal condition, become prominent in pathological states. For the cell infiltration originating in the sub-mucous tissue by pressure smoothes out the mucous membrane and renders evident the orifices of the glands of Littré. In the circumscribed infiltration a number of capillaries are present, and are most abundant in its centre.

Both in the lumen of the glands of Littré and also in that of the urethra, the presence of numerous mononuclear and polynuclear leucocytes indicates the existence of a suppurative process.

A proliferation of granulation tissue situated in the lumen of the urethra is of peculiar interest (i^2). On either side of this button-shaped projecting growth, resembling that observed in pharyngitis chronica, the epithelium suddenly ceases, and a profuse granulation tissue growth, made up of mono- and polynuclear leucocytes and plasma cells, but altogether destitute of mast cells, projects in a knob-like form from the connective tissue occupying the interior of the urethra. In this case also from the irregularly arranged disorderly cells of a soft infiltration, the organisation of a hard infiltration has arisen.

Plate IX. Fig. 22. **Molluscum contagiosum.**

× 105, Obj. 3, Ocul. 4.

ml = molluscous body, s = sweat gland, e = degenerated epithelium, k = keratohyalin, r = rete, strc = stratum corneum, strgr = stratum granulosum, g = vessels, h = hair.

A proliferation from the rete forms the foundation of this growth. From its point of origin the lesion may extend, forming a larger or smaller lobulated

growth. Hence the single lobule is not unlike the segment of an orange. The tumour is embedded in a tenuous fine-meshed connective tissue, which projects delicate off-shoots provided with minute vessels between the individual lobes.

Too much importance has hitherto been attached to the coarse macroscopical appearance of the tumour, and, on account of its lobulated aspect, the growth has been thought to be connected with the sebaceous glands. But this is certainly not the case, for the new epithelial formation undoubtedly originates in the rete; the luxuriant cells of the rete Malpighii display in the tumour most obvious degenerative features, so that the resemblance to an Epithelioma contagiosum, pointed out by Neisser, is striking.

At the periphery of the single almost similar lobes, a varied series of cylindrical rete cells is observed, which obviously display a dull-coloured nucleus and light protoplasm. In many cells the prickles which bridge over the intercellular spaces can still be made out. It is not unusual to find in this locality a process of mitosis and an epithelial thread formation. These latter disappear directly we proceed from the cylindrical cells to the interior of the lobules. Kromayer was the first to describe this crumbling and destruction of the protoplasmic threads. The cells here undergo marked change. They swell up and become from three to four times as large as the rete cells from which they have arisen. The protoplasm has become more markedly hyaline, and is therefore difficult to stain. The nucleus stands out prominently, and displays well-stained chromatin granules. It is remarkable that it is usually eccentric, as is seen in the plasma cells. C. Beck draws attention to the fact that the earliest indication of the cell change consists in the appearance of one or more small, bright, homogeneous, sharply-defined specks. In order to avoid prejudice, Beck contrasts this appearance with the customary molluscous bodies or vacuoles.

The more the interior of the lobules is left out of account, so much the more does the nucleus lose its original appearance and take on a cap form. At the same time the protoplasm shrinks, and in it a process of vacuole formation commences. According to the observation of Neisser, a horny mass is developed between nucleus and protoplasm, a parasite, the growth and further development of which push the nucleus to one side, and down into the epithelial cells. On the other hand Kromayer, by the employment of staining methods, has proved that this horny mass is, from the very first, a product of cell destruction. It becomes divided into irregular large ball-shaped fragments, from the union of which the firm molluscous bodies found in the newly formed corneous investment of the cells take their origin (Kromayer).

The more the inner portion of the tumour is neglected, so much the more it becomes evident that the cells are drawn out and take up keratohyalin abundantly at their poles. This formation of keratohyalin becoming continually more luxuriant, the cells are thus more homogeneous. The nearer the centre of the tumour is approached, the more markedly do all the lobules inpinge on one another to form a cavity, which is occupied by the uniformly swollen cast-off masses of cells manifesting no difference of structure. These last fattily degenerate cells project through the roof of the molluscum; they yield a distinct fat reaction with osmic acid, but do not display an absolute resistance to alcohol and ether, as also to vinegar and thin lye.

We have not been able to convince ourselves that the molluscous bodies are of parasitic nature. We think that they are rather the result of the hyalin or colloid degeneration of cells.

Gonorrhoea chronica.

Fig. 21.

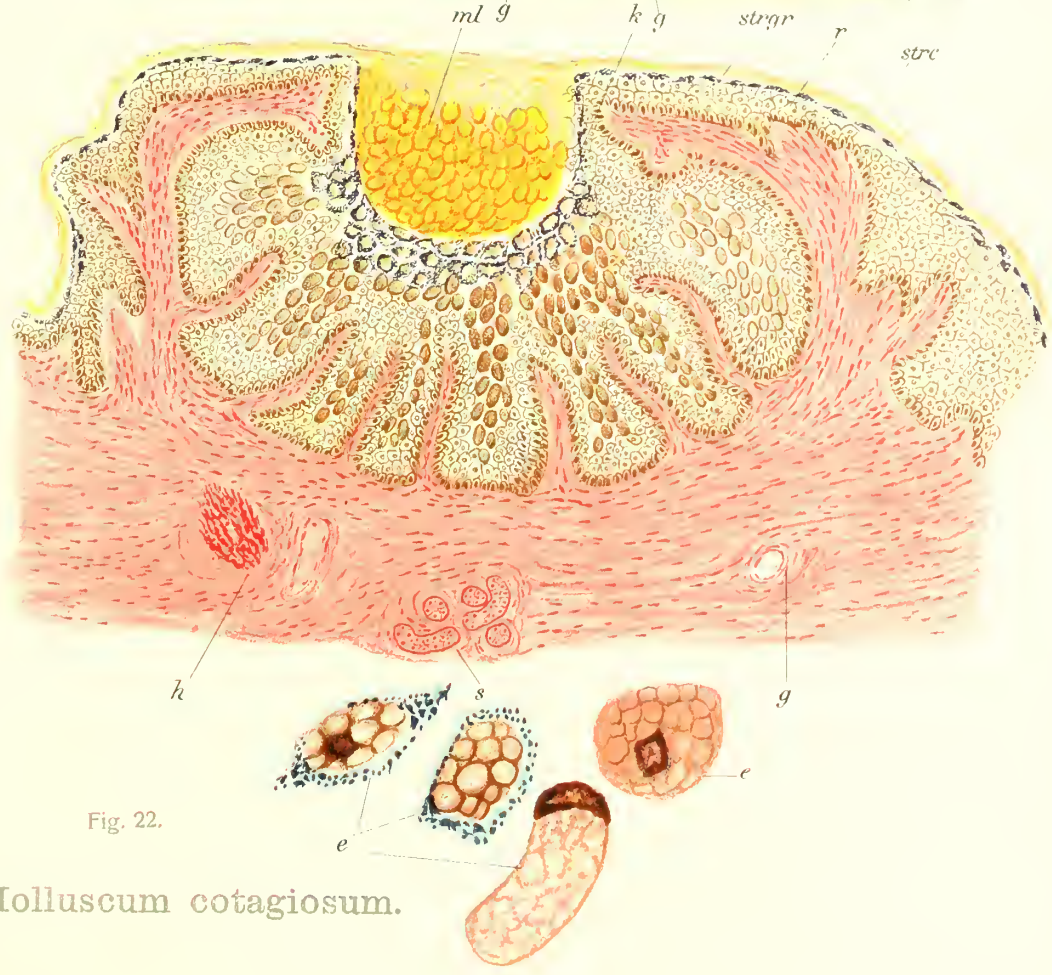


Fig. 22.

Molluscum cotagiosum.

Plate X. Fig. 23. **Ichthyosis hystrix.**

× 85, Obj. 3, Ocul. 3.

c = capillary, s = sweat glands, strc = stratum corneum, r = rete, b = connective tissue, g = artery, m = mast cells.

The luxuriant horny cones rise boldly from the epidermis. They partially run together into large plaques and partially stand out as sharply-defined, horny epithelial masses without any transition from the rete. Contrary to all other pure hyperkeratoses, the type of which is portrayed by ichthyosis, the characteristic feature is the sharp transition from the rete Malpighii to the epidermis. The papillary layer is normal, or is, perhaps, in several localities somewhat atrophied. Acanthosis, which is so often met with in warty formations, is entirely absent. The corium would seem to be somewhat atrophied, but inflammatory changes are very slightly marked. It is true that, around the dilated and especially the elongated papillary vessels, a slight leucocytosis may be detected, but this never assumes any marked development. Mast cells are abundant, especially in the vicinity of the vessels. Somewhat remarkable is the condition of the elastic fibre anastomosis which, in the upper third of the corium, has entirely disappeared, probably as the result of a peculiar degeneration, while in the middle and lower thirds of the corium the elastic fibres are clearly evident.

Between the rete Malpighii and the stratum corneum, keratohyalin cells are interpolated, for the most part in a single layer only. Should the method of hardening recommended by Ernst, Gram's method, be selected for the investigation, it will be possible to trace the direct transition from the keratohyalin to the keratin layer. The last consists exclusively of delicate, fine granules, which are located at the edge of the cell and stand out prominently from the unstained contents. It is worthy of notice that, contrary to what occurs in normal conditions, the oldest and strongest epidermic layers are most deeply stained by Gram's method.

Not only in the stratum cylindricum, but also in the upper portion of the corium is pigmentation present. The sweat glands, just as in other processes, *e.g.*, lichen, display a marked number of cystic dilatations.

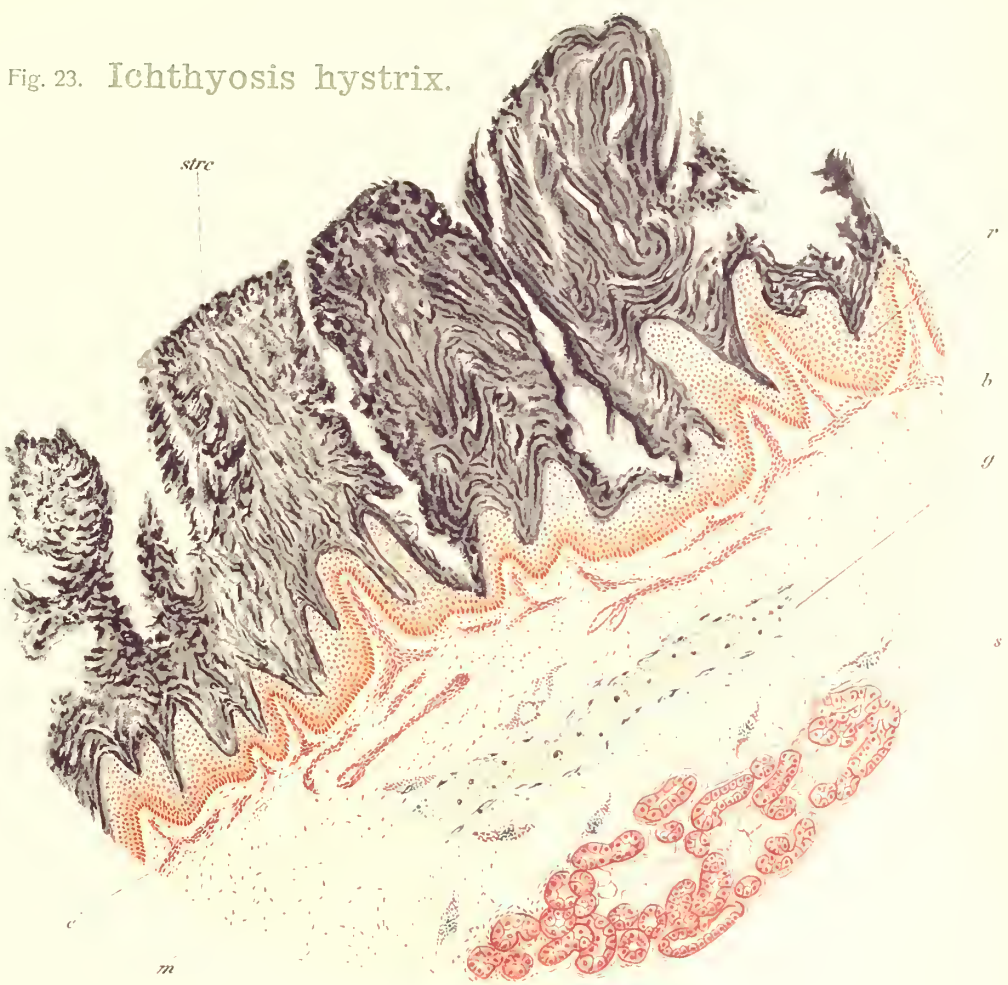
Plate X. Fig. 24. **Erythrasma.**

× 800, Oil immersion $\frac{1}{12}$, Ocul. 3.

The preparation is produced in the same manner as that employed when speaking of eczema. The active agent of the disease is here portrayed in the clearest possible manner; this active principle was first described by Burchard, and on account of the extreme delicacy of its elements has been named *microsporon minutissimum.*

The pure culture was first obtained by Vörner. The extreme tenuity of the mycelia and the gonidia would at the first glance suggest a comparison with the cocci. But it is quickly recognised that the mycelium bears the closest resemblance to that of the microsporon furfur, although scarcely a third of the size of the latter (Riehl).

Fig. 23. Ichthyosis hystrix.



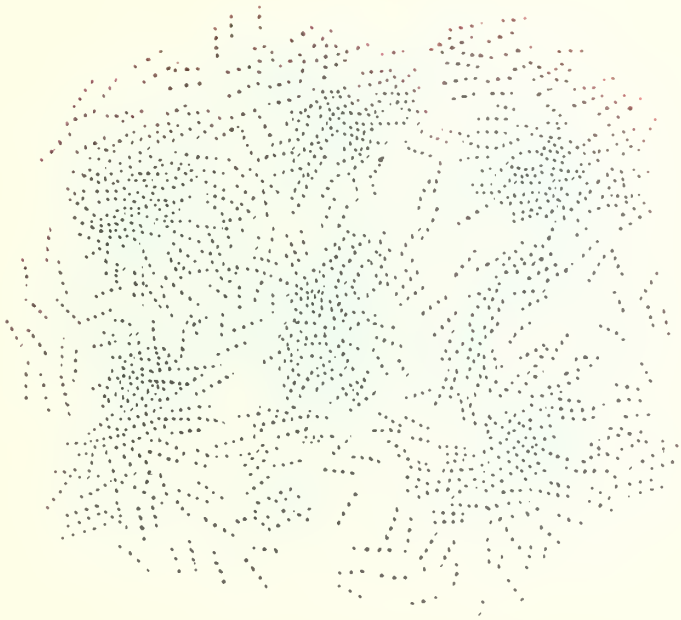


Fig. 24. Erythrasma.

Plate XI. Fig. 25. **Leukoplakia buccalis.**

× 85, Obj. 3, Ocul. 3.

p = epidermic perles, r = rete, g = vessel, b = connective tissue, strc = stratum corneum.

A concentrically disposed, laminated growth, prominently elevated from the epithelial investment, occupies a circumscribed area of the oral mucous membrane. As a proof of firmness of structure it will be noticed that, contrary to what is found in the normal pavement epithelium of the oral cavity, no trace of the presence of nuclei is detectable at the site of the growth. And the superficial epithelium is much hypertrophied. These horny masses penetrate the individual rete cones and compress them, so that they assume the appearance of epidermic perles in consequence of the strong pressure to which they are subjected.

Hence it is not surprising if, after this process has lasted some time, an atypical proliferation of epithelium should arise and the connective tissue be subsequently infiltrated with this epithelium. In other words, carcinoma may follow leukoplakia. In the figure only the early stages of the process are depicted, and no atypical epithelial overgrowth can be made out. The connective tissue offers a temporary resistance to the entrance of the epithelium, and thus the aggregations of the latter are especially prominent laterally towards the surface, where they experience the least resistance. Further, the rete itself displays overgrowth, but acanthosis is less definite and the connective tissue changes less marked. Some dilated capillaries, with trifling infiltration in their vicinity, are visible, but no marked inflammatory changes are present in the corium.

In later stages of the malady the whole mucous membrane, even as far down as the muscular layer, is the seat of an intense cell proliferation. Leloir maintained that, at the point where carcinoma commences, the stratum granulosum is wanting.

I find that the cells of the stratum granulosum which are present in mucous membrane with their abundant keratohyalin contents, cease to be met with quite suddenly in the locality where the leukoplakia begins. This may be rendered quite clear by the employment of Van Gieson's method of staining.

In these localities, when the elastin stains are made use of, it is immediately obvious that, deep down in the sub-mucous tissue, the system of elastic fibres is maintained in good condition. But in the upper portion of the sub-mucous tissue, in the papillary layer immediately beneath the rete, the impression is formed that the elastic tissue is very greatly rarefied, and in many places this tissue is altogether wanting. No wonder, therefore, if the resisting power of the collagen has also disappeared and hence the advance of the epithelial overgrowth is rendered more easy, and it is able more effectually to obtain a hold on the connective tissue. The result is the development of carcinoma.

Plate XI. Fig. 26. **Pityriasis rosea.**

× 105 Leitz, Obj. 3, Ocul. 4.

i = infiltration, bl = vesicle, h = hair, strc = stratum corneum, r = rete, b = connective tissue.

According to the published investigations of Löwenbach (*Vienna Klin. Woch.* 23, 1899), which were carried out in my Polyclinic, in the acute stage of this eruption are found: (1) a moderate parakeratosis, less marked in the epidermis, also acanthosis with slight inter-cellular œdema and leucocytosis. (2) Marked changes in the upper portion of the cutis, great infiltration of the papillary area, the effusion being sharply limited inferiorly.

In some preparations the epidermis is normal, in others it is raised up laterally; in many cases it contains scattered nuclei. In many points the stratum granulosum is wanting, in others it is present in the form of narrow, fusiform, granular cells. The rete cells are elongated and dilated, the sub-papillary prickle layer is also widened. The individual rete cells are somewhat enlarged and swollen, the inter-cellular spaces being dilated here and there. At many points the intra- and inter-cellular œdema has progressed to such an extent as to form vesicles (bl) beneath the epidermis; these contain serum and sero-cellular effusion. Here and there in the dilated inter-cellular spaces numerous collections of leucocytes are observed, and render ill-defined the boundary line between cutis and epidermis.

In comparison with the epidermis, the cutis manifests much more pronounced changes. The papillary and the sub-papillary layers are the chief localities in which the changes occur, and they extend also to the sub-papillary vascular anastomosis. The whole of this portion of the cutis is the seat of a pronounced infiltration, which is most marked around the individual vessels, but is by no means of small proportions in the whole of the region referred to.

The infiltration is composed of proliferated spindle cells of the cutaneous connective tissue, plasma cells, polynuclear and to a preponderant extent of mononuclear leucocytes.

Mast cells, on the contrary, are met with in very small number, and would indeed seem to be reduced below the normal. The collagenous and elastic fibres appear to be somewhat forced asunder by the infiltration. The latter, at the level of the sub-papillary anastomosis, terminates in a sharply defined line of demarcation. In some cases the infiltration follows the course of the vessels right down to the deeper layers, but the tissue itself does not display any departure from the normal; mast cells are here present in their usual number.

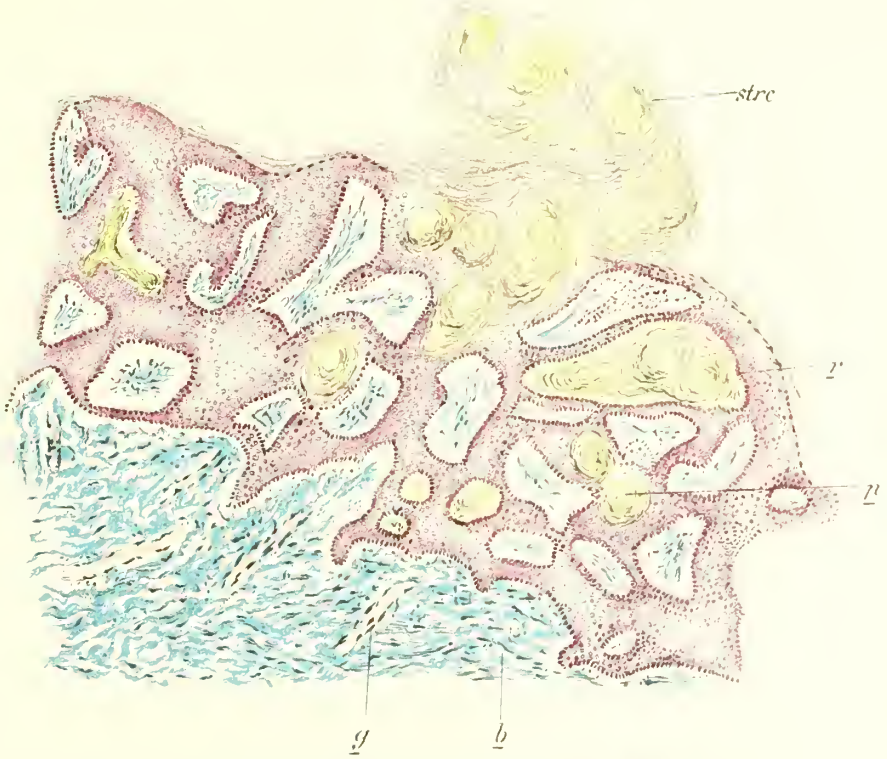


Fig. 25. Leukoplakia buccalis.

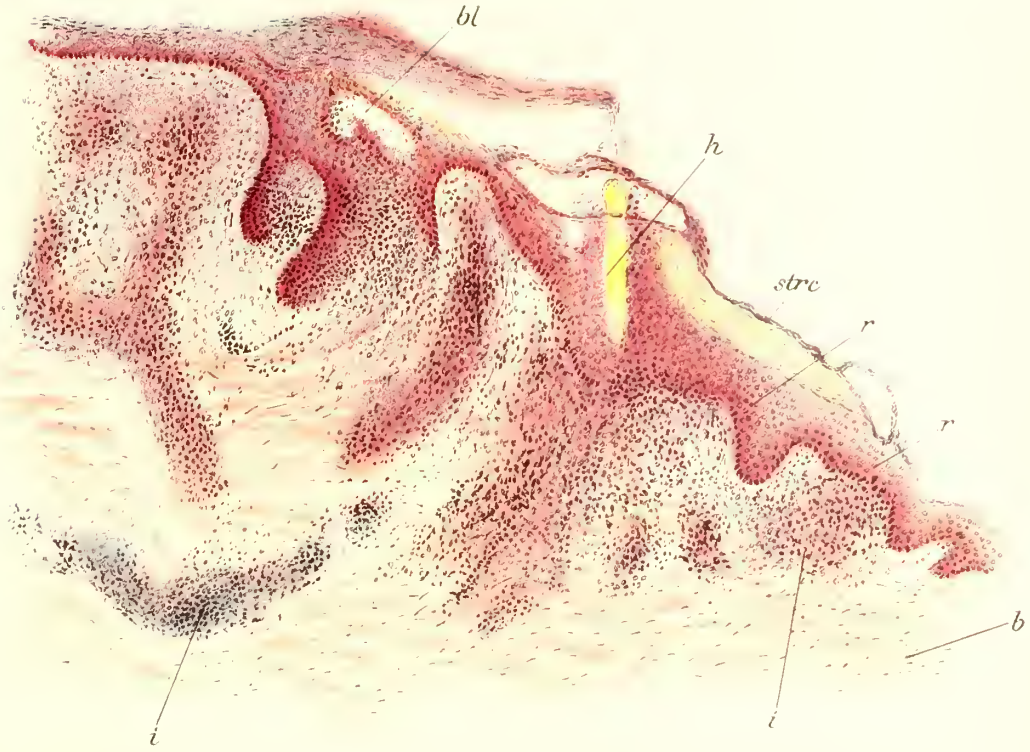


Fig. 26. Pityriasis rosea.

Plate XII. Fig. 27. **Lichen ruber planus incipiens.**

× 105, Obj. 3, Ocul. 4.

bl = vessel, l = overlapping nucleus, i = infiltration of leucocytes, r = rete, g = vessel, h = hair, b = connective tissue, strc = stratum corneum, strg = stratum granulosum.

In the very earliest stages during which the lichen papule is clinically detectable, indications of the later, more fully developed process, in the form of an elevation of the epidermis from the corium, are not wanting. A portion of the rete Malpighii which approximates the papillary layer, more especially the stratum cylindricum, is destroyed, and some rete cells are found in the cavities which have thus arisen, these cells being partly isolated, partly collected in heaps. Amongst the remains of the rete, which is still maintained on both sides in a normal condition, a glass-like clot, formed of fine fibrinous threads enclosing a number of leucocytes in their meshes, is found. Since Caspari (*Viertelj. f. Dermat. u. Syph.*, 1888, S. 159) and I (*Arch. f. Dermat. u. Syph.*, 1897, 38 Bd.) called attention to the engorgement vesicle (Touton) the pathological significance of this is universally recognised. Further, F. Pinkus (*Arch. f. Dermat. u. Syph.*, 1902, 60 Bd.) has detected a direct process of epithelial destruction at the boundary of the cutis, a solution of continuity of the uniting epithelial cells through a process of undermining.

In brief, the individual lichen papule usually occupies the space left by the destruction of several papillæ. Each papilla is extremely widened out, and contains a quantity of round cells, chiefly mononuclear leucocytes. But along with this flat, lentil-shaped infiltration of lymphocytes, Pinkus points out, as a most characteristic feature, the infiltration of the most superficial layers of the corium, right up to the epidermis with overlapping nucleated cells. He emphasizes this wandering of polynuclear leucocytes to the epidermis, and their penetration of the latter, as being a feature quite special and peculiar to Lichen ruber.

It seems to me that the infiltration proceeds from the vessels, for it is noticeable that in those papules which do not yet manifest any marked infiltration of the papillary layer, evident vascular changes are nevertheless present, and these are more marked in the deeper portion of the corium; this observation confirms that of Török (*Beitr. z. path. A. u. allg. Path.*, 1890, Bd. 8), and Lukasiewicz (*Arch. f. Dermat. u. Syph.*, 1896, Bd. 34). Here are discernible far more clearly than in the upper layers, not merely small, but also medium and, indeed, large vessels, whose walls are much thickened and surrounded by a well-marked layer of leucocytes. The vessels stand out prominently as thick elastic strands, and this not merely when observed in longitudinal section, for if the surface cut at right angles is examined, it will be noticed that the intima is thickened and penetrated by a certain number of leucocytes, while in the vicinity of the vessel a still larger number of the latter are visible. Thus in the early stage of papule formation, only a peri-vascular infiltration is detectable. At a later stage the process, extending from the point of origin, involves the tissue generally. A

formation of epidermis covering each individual papule ensues, but it attains only moderate proportions. The individual cells are strikingly hypertrophied, almost as much so as those which cover the acuminate condylomata. As a result of this hypertrophy of the epidermis on the one hand, and of vesicle formation on the other, the rete is in many points quite flattened out. Unna lays special stress on this feature as being particularly valuable in diagnosis.

In the more chronic lichen papules, to such an extent is the formation of vesicles carried that the appearances portrayed in my Textbook of Skin Diseases (5th ed., Leipzig, Thieme, 1905, S. 91) are produced. The infiltration of the corium is fairly marked and the sweat glands display a cystic degenerative dilatation of their lumen. It is only the sebaceous glands and hair follicles which preserve their normal condition.

Plate XII. Fig. 28. **Lichen syphiliticus.**

× 85, Obj. 3, Ocul. 3.

h = hair, i = infiltration, b = connective tissue, g = vessel, s = sweat glands, r = rete, ri = giant cells, p = plasma cells, strc = stratum corneum, strg = stratum granulosum.

The preparation is taken from the case, an account of which has been published in my *Dermat. Zentralblatt* (3 Jahrg., Jan. 1900) by Hirschlaff. Whilst the epidermis is slightly raised, in the corium a fairly sharply-defined infiltration of epithelial and lymph cells is met with according to the investigations of Kaposi, J. Neumann, Griffini, and Michelson. Often, but not invariably, the infiltration is located around a hair follicle. Some giant cells are observed in the centre, so that the nodule bears a certain resemblance to a bacillus containing tubercle; a numerous collection of plasma cells forms a striking feature in the vicinity. Neither Michelson nor Hirschlaff has been able to discover tubercle bacilli, and the latter observer has not succeeded, by inoculating the contents of a tubercle on guinea-pigs, in causing a subsequent outbreak of a general tuberculosis. The possibility of a mixed infection of syphilis and tubercle, which some are supposed to think may occur, is also clearly out of court.

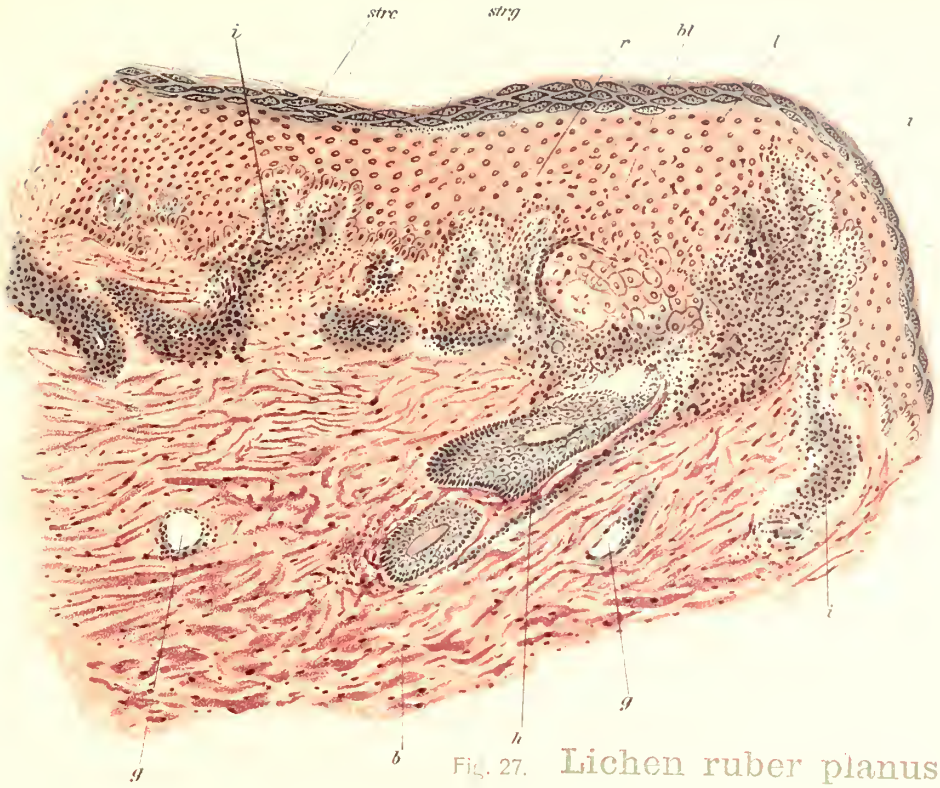


Fig. 27. Lichen ruber planus.

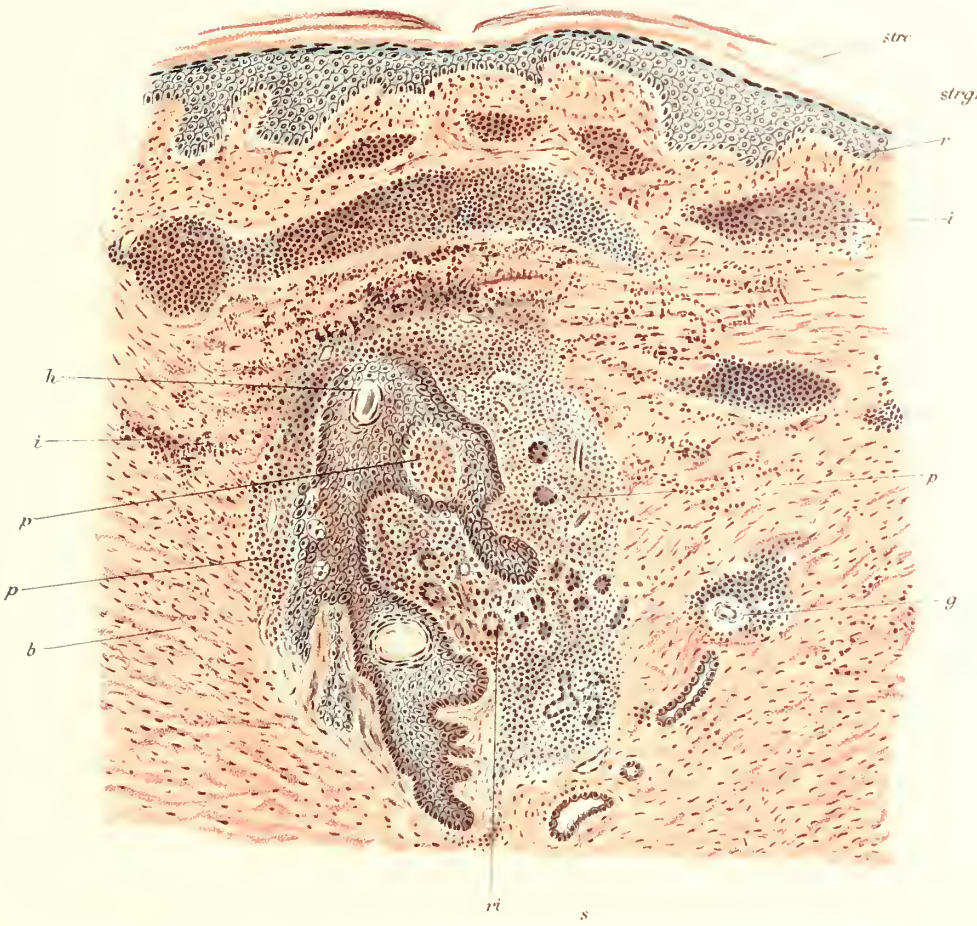


Fig. 28. Lichen syphiliticus.

Plate XIII. Fig. 29. **Lichen ruber verrucosus.**

× 105, Obj. 3, Ocul. 4.

bl = vesicle, c = overlapping nuclei, e = eleidin, i = infiltration, b = connective tissue, strc = stratum corneum, strg = stratum granulosum, r = rete.

From the histological aspect the morbid process may be divided into two stages. In the first stage, which is the subject of the present figure, the stratum corneum is extremely hypertrophied and arranged in definite lamellæ with separately stained nuclei; it contains abundant eleidin. Further, the stratum granulosum is here and there increased in thickness by from four to five layers owing to the presence of cells.

Just as in Lichen planus, so here also there is a marked elevation of the epidermis from the corium, and the vesicle is here again filled with a fine fibrinous network with a few leucocytes. The stratum dentatum and the stratum cylindricum are also somewhat hypertrophied, and between the individual cells numerous overlapping nuclei are perceptible.

Instead of the similar, highly developed hyperkeratinisation met with in ordinary warts, in Lichen verrucosus a dense infiltration of the corium occurs. Both as regards its thickness and diffusion, this infiltration resembles that observed in Tuberculosis verrucosa cutis, but giant cells are wanting, as are also all other cells suggesting the presence of tubercles. On the other hand, the papillæ are often remarkably lengthened, narrow, threadlike, and irregular. The vessels of the papillary layer are dilated, and the infiltration is made up of mononuclear leucocytes, amongst which a few mast cells can be detected. Towards the sub-papillary layer of the corium, the thickness of the infiltration greatly increases, and within the large cell masses are here frequently found kariokinetic figures, as also numerous mast cells. The cells forming the infiltration are irregularly distributed, but chiefly in the vicinity of the vessels. As occurs also in Lichen planus, cystic dilatations of the coiled ducts of the sweat glands are present. Especially noticeable are the projecting epidermic cones which in many places penetrate deeply into the corium and in others stand out prominently, recalling those met with in the plates representing Pityriasis rubra pilaris.

In later stages of the malady the tendency to ultimate atrophy may be recognised both histologically and clinically. The epidermis is quite normal and the diffuse cell infiltration of the corium takes on a string or bead-like arrangement between the bundles of connective tissue. The series are separated by remarkably long and narrow capillaries.

I think further that, as in Lichen rubra planus, the inflammation of the corium extends from the vessels and is followed by an infiltration in the superficial layer of the cutis, while hypertrophy of the epidermis ensues as a secondary result. The more markedly this inflammatory process in the corium manifests a tendency to shrinking, the more abundantly connective tissue formation ensues, so much the more is hyperkeratosis in evidence.

Plate XIII. Fig. 30. **Lymphangioma simplex.**

× 105, Obj. 3, Ocul. 4.

t = lymph space, e = endothelium, r = rete, i = infiltration, h = hair, b = connective tissue, g = vessel, strc = stratum corneum.

By the courtesy of my colleague, Herr Peter, of Königsberg, I am enabled to reproduce this preparation. The individual nodules project from the surface of the skin, resembling small tumours; each nodule is easily recognisable from the presence of a considerable number of larger or smaller cavities lined with smooth flat epithelium, these cavities being connected with the lymphatics of the superior and inferior portions of the corium. There can be no doubt that the lesion partakes of the nature of a Lymphangioma simplex cysticum.

The excellent description which Török (*Mon. f. Prakt. Dermat.* 14, 1892) has given of the simple lymphangiomata applies also to the present case:—"At many points the epidermis displays passive changes originating in previous alterations which have taken place in the papillary layer. The epithelial crests are compressed and abbreviated and sometimes entirely destroyed, and the stratum of prickle cell is frequently reduced to two layers. Yet some of the epithelial crests are proliferated. The most important histological changes, however, are those involving the papillary and sub-papillary layers of the corium, in which a development of tortuous canals and wide cavities is in progress. These cavities in the papillæ usually assume a round, oval, or pear shape; they are often also very irregular and pass over at the base into one, seldom two, somewhat dilated capillaries. In the sub-papillary layer the cavities are smaller, and of a more irregular form. These cavities also present varicose dilatations of the capillaries. Through a similar well-marked dilatation, wide, closely twisted tubes arise, the convolutions of which are perceptible in the section as cavities of unequal size merely separated from one another by their septa. Through continuous increase of size the closely compressed convolutions encroach on the septa, and contiguous sections of tubes coalesce, with the result that the remainder of the dividing partitions project into the lumen as spur-like processes. In this way indented or cylindrical cysts may be gradually formed in the convoluted and widened canals. The cavities are covered with flattened endothelium, and a columnar endothelium is sometimes found."

Török has rightly laid stress on the fact that the whole process is hyperplastic. So if the basis thereof be a single ectatic dilatation of vessels, it is clear that the endothelium would be everywhere flattened, and the nuclei of the same markedly compressed. As evidence of the process being one of new formation may be adduced the fact of the lymphatics travelling to the apex of the papillæ, where in the normal condition, the latter either contain no lymphatics, or else these are scattered here and there only in the lower third.

Underneath the wart-like projecting tumour only a few collections of cells are visible, while in the cavities fine granulated coagulated lymph, with some few white blood corpuscles, is present.

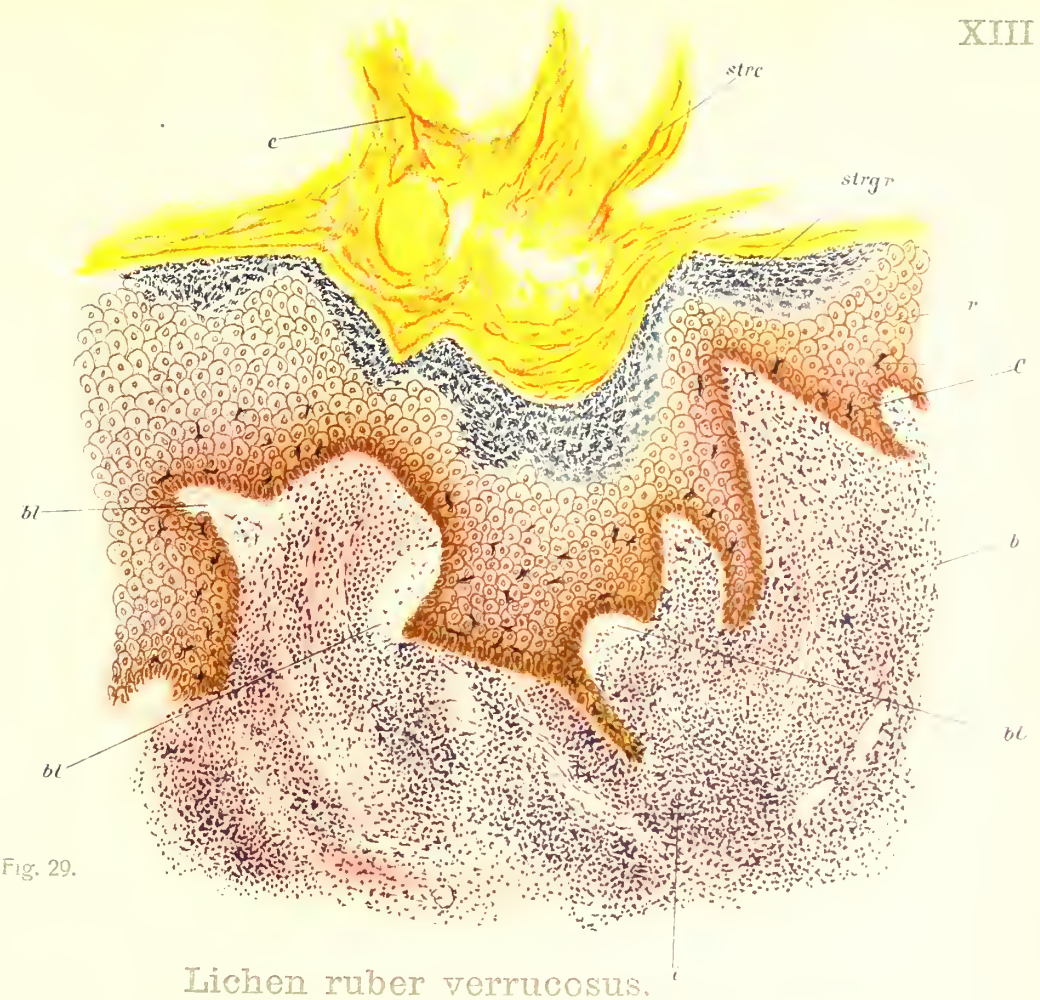


Fig. 29.

Lichen ruber verrucosus.

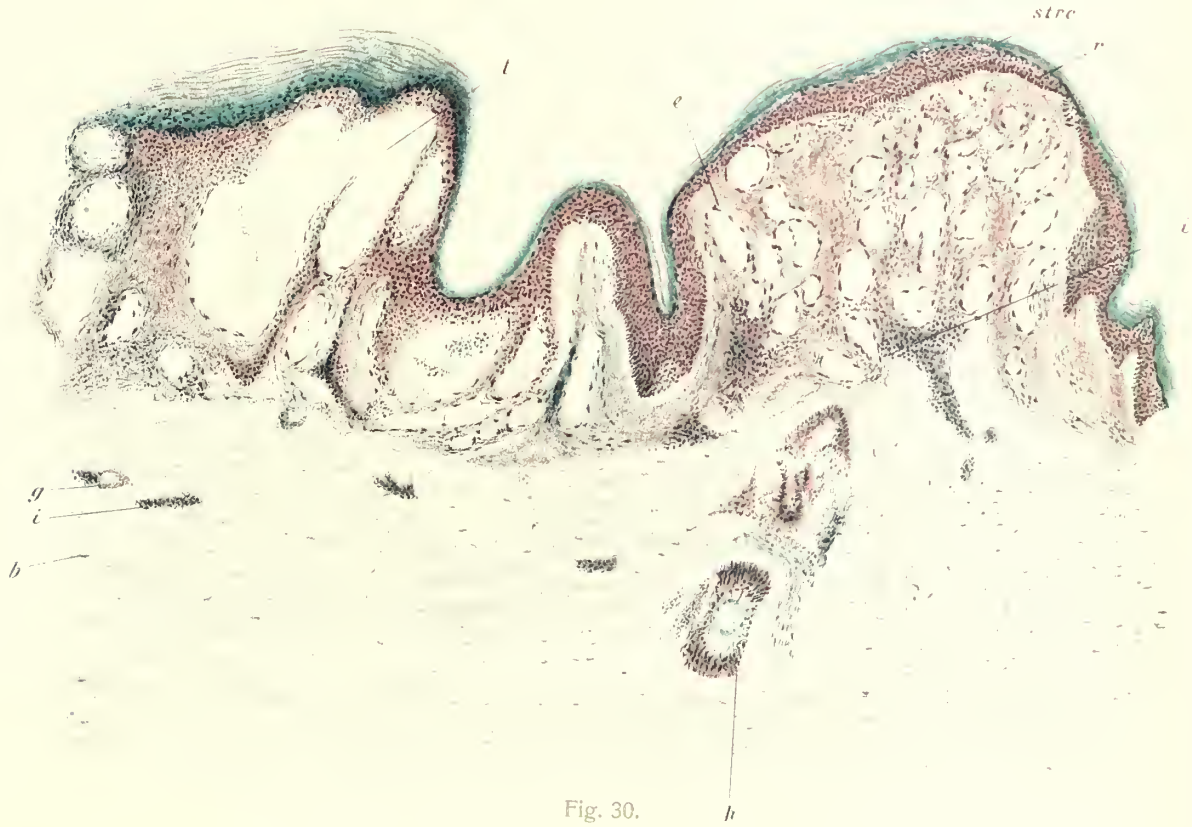


Fig. 30.

Lymphangioma simplex.

Plate XIV. Fig. 31. **Lupus erythematosus.**

× 85, Obj. 3, Ocul. 3.

ch = scale, c = cocoon with cocci. The cocoon × 800, oil immersion $\frac{1}{12}$, Ocul. 3, m = mast cells, strc = stratum corneum, r = rete, i = infiltration, d = demodex folliculorum, t = sebaceous gland, a = vessel, s = sweat glands, h = hair sheath.

The most prominent and striking feature of this figure is the marked infiltration which is present in the corium, and more particularly in the upper and middle layers, and in the sweat and sebaceous glands. This infiltration is made up almost entirely of mono-nuclear leucocytes, but few poly-nuclear cells are present, and there is a striking paucity of plasma and mast cells. The collagen is swollen from œdema, and its vessels are much dilated. Here and there the infiltration is so dense that the elastic fibres contained within it have completely disappeared, or are only to be recognised by the staining process. I have not succeeded in detecting the colloid degeneration of the elastic fibres in the early stages of the disease from which the preparation is taken, as described by Schoonheid (*Arch. f. Dermat. u. Syph.* 54, 1900).

In comparison with this involvement of the corium, the epidermic changes occupy but a subordinate position. A slight necrosis is to be made out at certain circumscribed points. The stratum granulosum is normal, and the rete displays a somewhat marked acanthosis in many places. Numerous mitoses are here in progress, and, as occurs in many inflammatory conditions, the peculiar nucleus degeneration described by Unna as " chromatotexis " (ch.) is discernible.

With this is connected a curious and quite special thickening of the epidermis, with marked parakeratosis, which is particularly evident as regards the excretory ducts of the follicle. These are also filled with large quantities of cocci, which must certainly be regarded as the result of a secondary invasion. Yet these cocoons of ordinary cocci are peculiar to lupus erythematosus in that they are not to be met with in all and every inflammatory disease of the skin.

I must not omit to point out that the above described limitation of the inflammatory process to the sweat and sebaceous glands is of great clinical importance, for the resulting fresh local scarring tends to produce complete atrophy of the follicles and sebaceous and sweat glands, which must obviously remain permanently.

Plate XIV. Fig. 32. **Lupus vulgaris.**

× 85, Obj. 3, Ocul. 3.

k = chromatotexis, ri = giant cells, i = infiltration, p = plasma cells, t = tubercle, e = epithelioid cells, str = stratum corneum, strg = stratum granulosum, r = rete, g = vessel.
The giant, epithelioid, and plasma cells are × 800 (Ocul. 3, Oil immersion $\frac{1}{12}$).

The view that lupus is a local tuberculosis of the skin is at the present time universally held to be correct, and that this is so is most clearly obvious from an examination of the accompanying figures. There is here displayed a slight acanthosis, and in the upper portion of the corium two miliary tubercles, one only partially seen, are situated. In the miliary tubercles a large number of giant cells (*ri*) is found. In the vicinity of the giant cells, plasma cells (*p*) are observed, and, as evidence of the action of the toxin appertaining to the bacilli, it will be noticed that the connective tissue cells are converted into epithelial cells (*e*) possessing a large nucleus. Finally, in the vicinity of the miliary tubercles an infiltration of leucocytes is present, an evidence that the tubercle acts on the tissue to some extent as a foreign body. This peripheral infiltration of round cells renders indistinct the transition between tubercle and connective tissue, as Kreibich points out. The leucocytes are for the most part furnished with round nuclei and are of small size. The cell-body is very small, often scarcely perceptible ; the nucleus is rich in chromatin, and its staining is diffuse. The leucocytes lie in the masses of the reticulum.

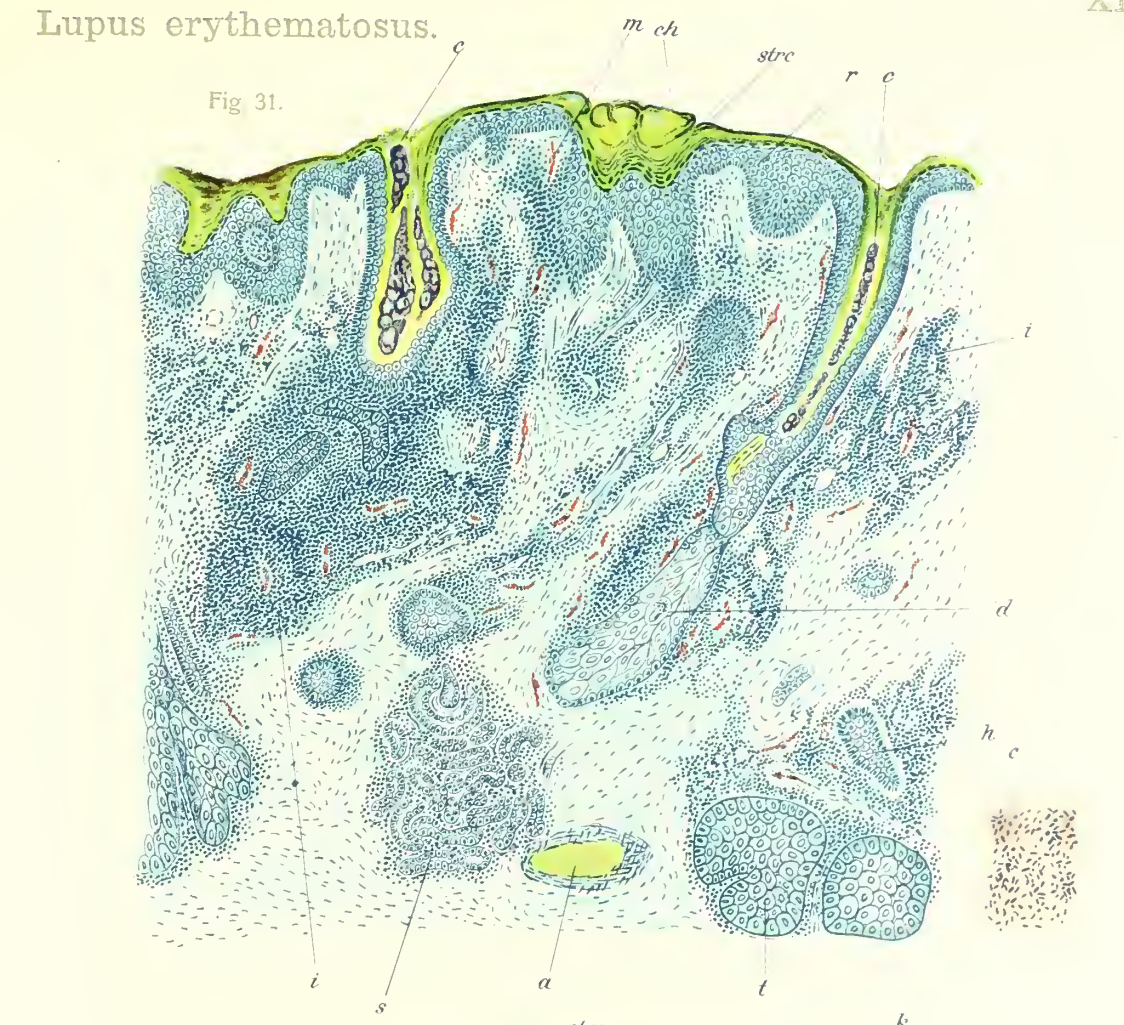
When a higher power is used the typical giant cells of Langhans stand out prominently; their wreath of from ten to twenty nuclei at the periphery and the coagulating necrosis in the centre are very obvious. The giant cells are derived partly from the autochthonous tissue, partly from the endothelial portion of the capillary wall, and that of the new-formed vessels of large calibre (Brosch). The origin of the tubercle was in the first instance attributed by Baumgarten to proliferation of the fixed connective tissue cells; later, however, it was proved by Kockel that the proliferating endothelium of the vessels was converted into epithelioid cells, and that therefore no new capillary can be formed. For this reason tubercle is devoid of vessels.

In such giant cells here and there one or two bacilli are found, especially at the periphery of the non-nucleated portion ; according to Weigert, especially at the periphery of the nucleus, and between the nuclei.

The plasma cells are distinguished by the fact that the wheel-shaped nucleus is placed eccentrically, and the protoplasm is obviously granular. In Lupus vulgaris mast cells are present in small numbers only. The new growth is particularly amenable to staining with Unna's polychrome methylene blue. It acts metachromatically, the mast cells becoming red and the plasma cells blue. In lupus, as in other infectious inflammations, a peculiar degeneration of the nucleus is often present. This Unna describes as nucleus dissolution, " chromatotexis " (K).

Lupus erythematosus.

Fig. 31.



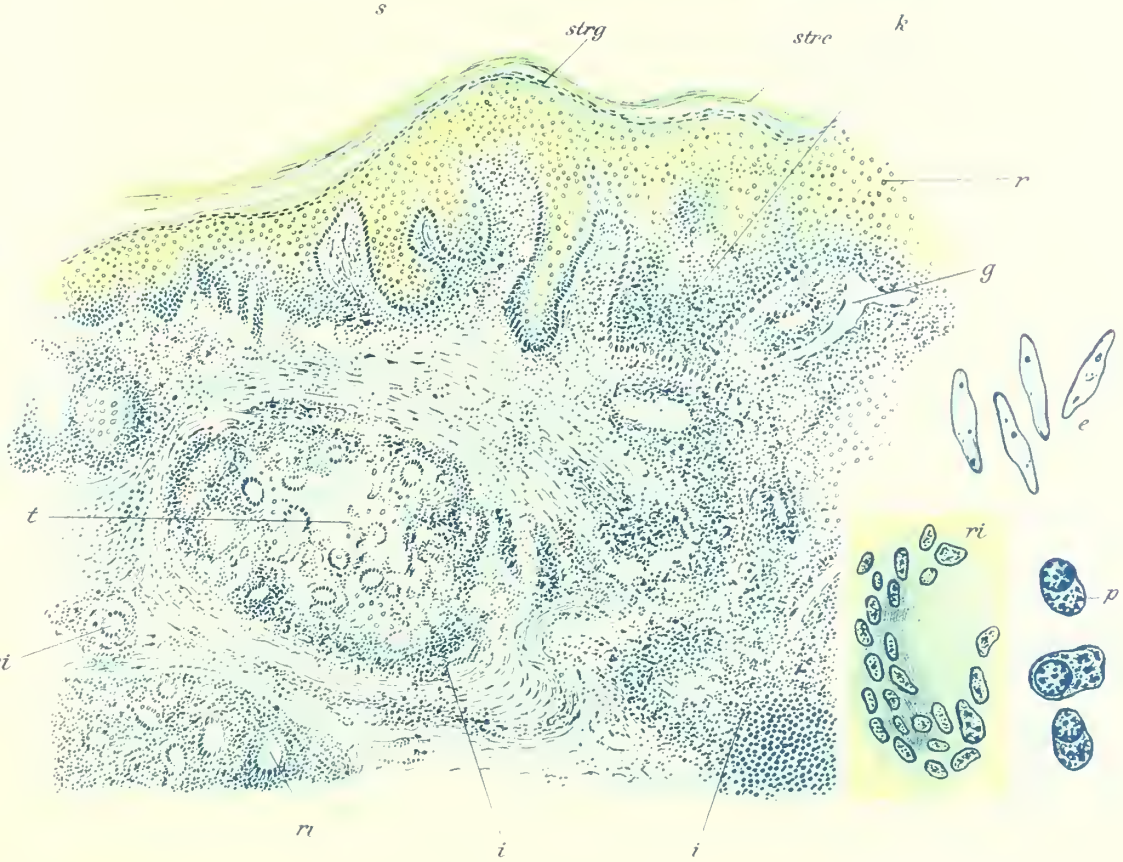


Fig. 32. Lupus vulgaris.

Plate XV. Fig. 33. **Mycosis fungoides.**

× 85, Obj. 3, Ocul. 3.

bl = vesicle, l = lymph plates, pg = pigment, i = infiltration, g = vessel, p = plasma cells. The latter × 800, Ocul. 3, Oil-immersion $\frac{1}{12}$.

The histological study of this remarkable malady leaves us just as much in the dark concerning its nature as does clinical observation. The most striking feature is the resemblance of the cell formation in this disease to that of sarcoma. Yet, when accurately studied, it becomes clear that many points adequate for differentiation of these maladies can be made out. Apart from the fact that mycosis fungoides differs from sarcoma inasmuch as metastases very seldom occur in the former, and inasmuch as the prompt administration of arsenic may cure the disease, which is never the case in sarcoma, the histological differences are sufficiently marked to enable the distinction between the two affections to be made.

In the first place, in mycosis fungoides the new growth progresses slowly from the deeper portion of the corium to the papillary layer, whereas in widespread and firmly established sarcomatosis a portion of the upper third of the corium still remains free from the new formation. In mycosis fungoides the process of cell formation extends to the extreme limit of the papillary layer, and the rete cones are often so closely welded that they present an epithelioma-like aspect.

The nature of the cells of the new formation is extremely diverse, and this polymorphism of the cells contrasts with the uniform character of those in sarcoma. Most usually a large number of cells, which are arranged in rows and contain scanty protoplasm and whose nucleus is furnished with a very variable quantity of chromatin, is met with. The younger forms with smaller nuclei contain tightly compacted chromatin, and the nuclei are therefore darker in tint. As age increases the nucleus becomes larger, vesicular, and then the staining becomes less marked. The cells insinuate themselves into the chinks of connective tissue without causing structural damage to the latter. No degenerative changes can be made out with appropriate staining of the connective tissue, *e.g.* by the van Gieson method.

While mast cells, though not very abundant, are still present, sarcomatous processes are entirely absent; the richness of the section in plasma cells is very striking, and pigment cells furnished with coarsely nucleated yellow-brown pigment, some of which are round others furnished with long processes, are present in the upper layers of the corium.

The cellular new formation is permeated with numerous elongated and widely dilated vessels, and between them are perceptible, contrary to what holds in sarcoma, many extremely delicate and tense elastic fibres.

The upper layers of the cutis must be regarded as the seat of election of the infiltration, for in this locality more marked karyokinetic figures are observed than in the lower layers. But all evidences of inflammation, in the sense of

Cohnheim's use of the term, are wanting, and here we are at one with Paltauf, for precedent emigration processes do not occur, and the accumulation of polynuclear round cells in and around the vessels, even where a rapid growth of the tissue is rendered evident by the numerous mitoses, is not observed.

But an essential characteristic of mycosis is that a persistent destruction of cells occurs. These together with the effusion are met with in the chinks and fissures with which the epithelium abounds. This pressing asunder attains its extreme degree in the formation of small intra-epithelial vesicles (bl), which, constituting the superficial covering, support merely the thin epidermis. These vesicles are distended with epithelial and infiltration cells, as also with cell débris.

When these vesicles are destroyed, large numbers of micro-organisms are observed in the ulcerated region. I agree with Paltauf in considering that the facility with which the tissue of mycosis fungoides is attacked by extraneous parasites is really astonishing. Yet the entrance of micro-organisms must be regarded as a purely secondary occurrence.

I agree with Paltauf that the mycosis nodules take their rise in connective tissue; the cells are all the descendants of connective tissue cells, and the reticulum arises from the original cutis tissue, in which, indeed, no granulation tumour pre-exists. What the essential nature of the disease may be remains, however, altogether problematical.

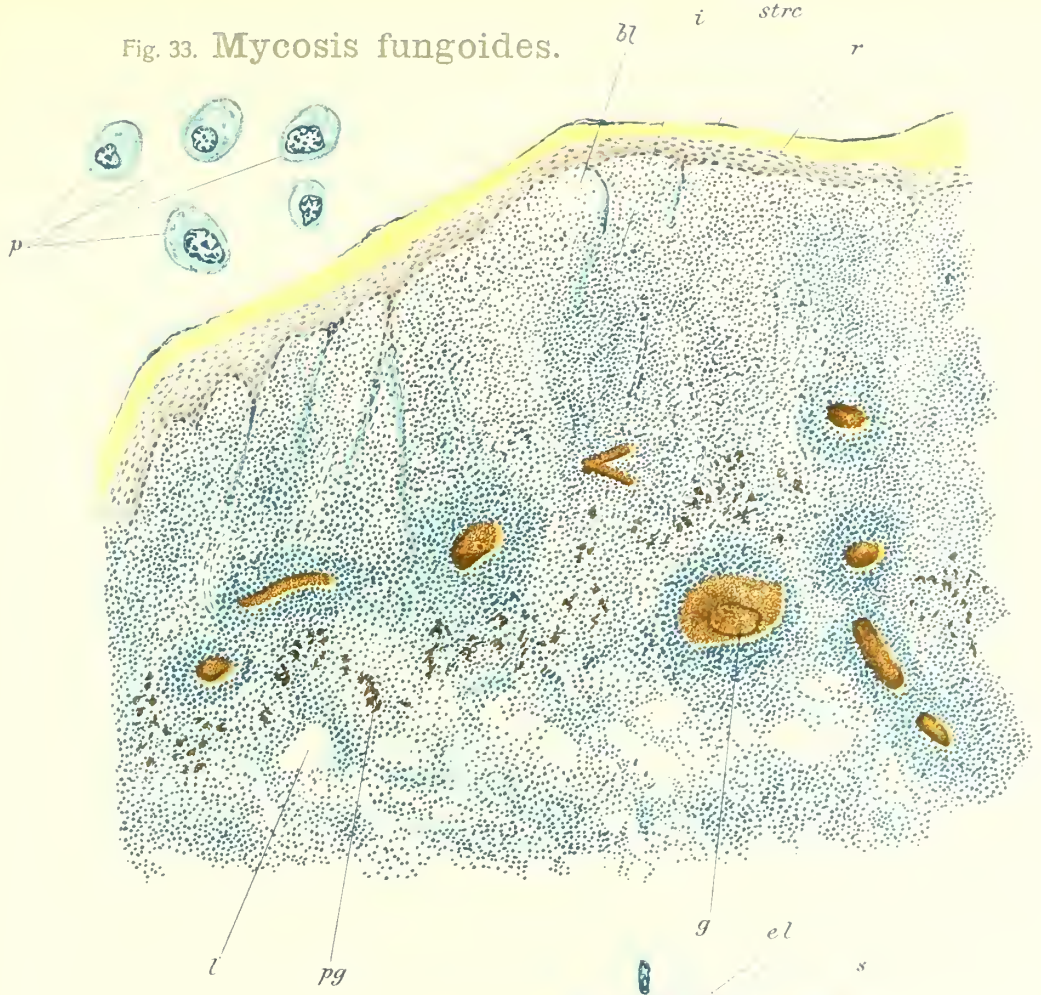
Plate XV. Fig. 34. **Eczema marginatum.**

× 1000, Oil-immersion $\frac{1}{12}$, Ocul. 4.

s = staphylococcus, h = yeast cells, el = desquamated epithelium, t = tricophyton tonsurans.

The preparation has been treated in the following manner: the fragments of superficial tissue removed with the sharp spoon were placed for 24 hours in a mixture of alcohol and ether, then a portion was stained with Löffler's methylene blue, and examined microscopically. It will be observed that this disease is really a combination of eczema with the trycophyton; in proximity to the trycophyton tonsurans with its abundant spores and mycelium, a quantity of torulæ and staphylococci together with desquamated epithelium are observed.

Fig. 33. Mycosis fungoides.



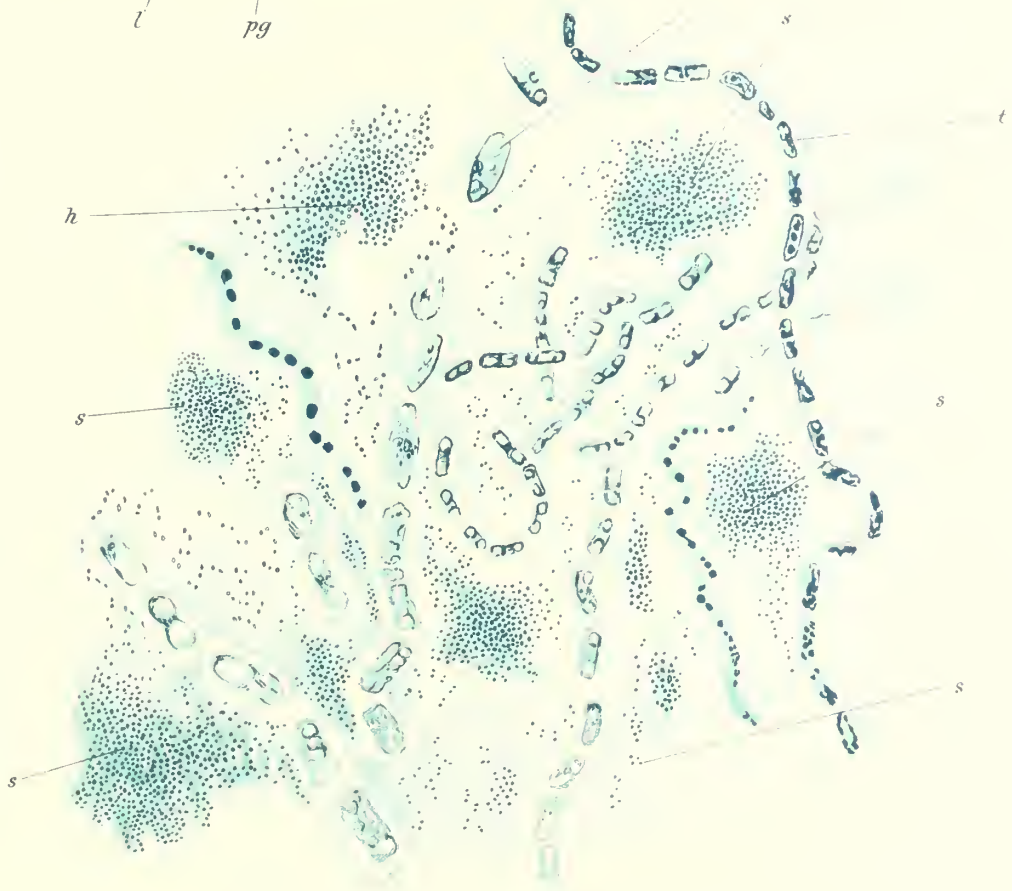


Fig. 34. Ekzema marginatum.

Plate XVI. Fig. 35. **Nævus congenitus.**

× 480, Obj. 6, Ocul. 4.

n = nævus nests, e = elastic fibres, r = rete, strc = stratum corneum, g = vessel. (This plate was most kindly placed at my disposition by my former assistant, Dr. Dreyer of Cologne.)

From the clinical standpoint the term nævus includes small tumours of the most various kinds; the feature common to them all is that they are congenital. Between the clinical and histological definition of these tumours there is great and striking incongruity. For histologically the only congenital tumours which can be classified as nævi are such as are the seat of an extraneous deposit in the corium of cell nests and columns. Thus fibroma, angioma, soft warts, &c., are excluded, although these may clinically be placed amongst the nævi, inasmuch as they are congenital.

These cell nests and columns stand out prominently in sections stained with orcein and polychrome methylene blue. They are here, as almost universally, separated from the epithelium by a layer of normal connective tissue, and in this, as also in the separate aggregations of cells, a number of most delicate elastic fibres are observed. These nests and columns of cells have a great theoretical importance, for they furnish the most satisfactory proof of the accuracy of Cohnheim's theory that, even in the embryonic condition, a series of malignant tumour elements is deposited, but remains in a quiescent condition unless and until the cells are stimulated to luxuriant growth through some irritation. It is regrettable that the author of this formidable theory has not investigated the innocent nævi from this special point of view. It is a well-ascertained fact that in some instances malignant tumours develop from these innocent growths; it is clear that these tumours take their origin in certain cell aggregations deposited *ab ovo*.

Whilst it was formerly held that these malignant tumours must ultimately be classed with the sarcomata, and that therefore the cell nests must have a mesodermic origin, yet Unna considered he had proved that, as a matter of fact, the groups of cells present in the corium arise primarily from the ectoderm and from the epithelium. He held that the epithelial character of these cells was proved in several ways, and that they in their fœtal state, from the superficial epithelium, had been transferred to the corium.

However attractive this theory may be, I cannot but think that it is too partial. As the result of numerous investigations carried out on many nævi, I have come to the conclusion that, as regards many tumours, the theory of Unna is correct, and that from such nævi carcinoma may be developed, these being also exceptionally pigmented. But in other cases the origin of nævus cells in the connective tissue is quite indisputable, and then may arise sarcomata of the most malignant type, *i.e.*, the pigmented variety. Finally, I am certain that nævi are met with the epithelial nests of which are of endothelial origin. Very possibly it is in this way that the extremely rare cases of cutaneous endothelioma originate.

In the case depicted, there can be no doubt that the cell nests are of ectodermal origin. With the comparatively low power employed in the figure this

fact does not very strikingly stand out; hence for the most part merely the nuclei of the cells can be recognised. Only in the lowest nævus network, in the immediate vicinity of the infiltration of leucocytes, the epithelial character of the polygonal cells with their vesicular nucleus can be recognised.

Plate XVI. Fig. 36. **Purpura rheumatica.**

× 85, Obj. 3, Ocul. 3.

s = sweat duct, g = sweat gland, ge = vessel, e = erythrocytes, l = leucocytes, f = fatty tissue, h = hair, strc = stratum corneum, strg = stratum granulosum, r = rete.

The preparation is taken from the leg of a girl of sixteen. The hæmorrhages are perceptibly limited to the upper portion of the papillary layer, and when van Gieson's method of staining is made use of, the hæmorrhage is clearly distinguishable from the beautiful red tint of the connective tissue. The hæmorrhage into the connective tissue chinks is that from the vessels which are widely dilated, a condition never observed normally in this superior portion of the skin. Thus the *vis a tergo* has become so powerful that some of the threads of connective tissue have been torn across, and in the cutis masses of red blood corpuscles with but few leucocytes are observed to be collected in irregular partitioned-off spaces. The hæmorrhages being quite fresh, they still display a bright red colour; the elements of the blood are very regularly arranged. At a later stage the red colour gradually changes to yellow, and finally the dissolved hæmoglobin stains the adjacent connective tissue bundles a yellowish tint. In the interspaces of the connective tissue, the so-called phantom images of the red corpuscles, "Schattenbilder," are observed. At those points in which strong strands of connective tissue form supports for the stroma, the hæmorrhage is arrested in its progress, *e.g.*, the sweat gland ducts and the hairs. And also between the rete and the hæmorrhage a sharp line of demarcation is visible. The connective tissue is in any case only passively involved and forced asunder by pressure. With van Gieson's stain it displays a bright red tint, and no chemical change into collastin or collacin has taken place.

Fig. 35. Naevus congenitus.

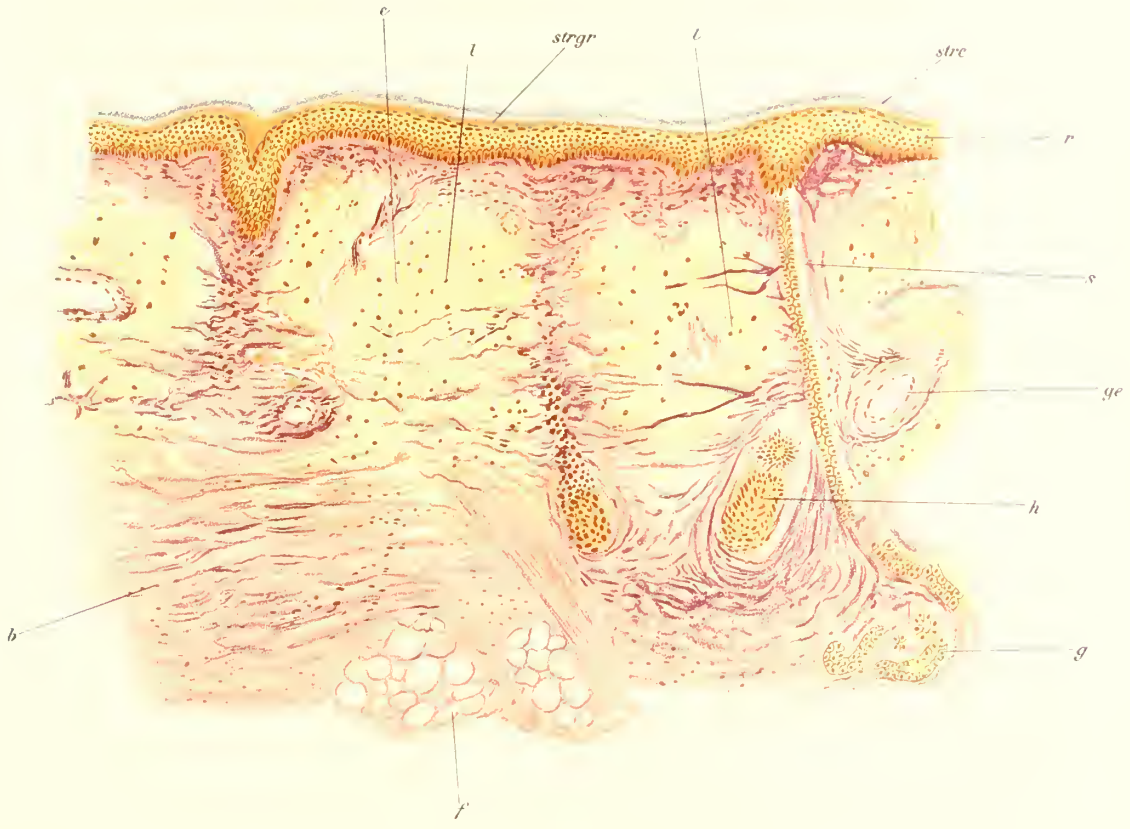


Fig. 36. Purpura rheumatica.

Plate XVII. Figs. 37 and 38. **Nævus sebaceus faciei.**

× 105, Obj. 3, Ocul. 4.

strc = stratum corneum, r = rete, h = hair, n = nævus nests, t = sebaceous glands, a = acarus sive demodex folliculorum.

The nest is × 625 (Obj. 7, Ocul. 4), and is represented lengthwise and in cross section.

I have shown above that in nævus the histological diagnosis is a relative one. In the clinical sense the tumours are understood to be small and congenital; histologically, cell nests and columns are detected in the corium, which have been present *ab ovo* and will remain there unaltered for the whole of life, or will develop into malignant tumours.

Now we have to deal with forms of nævus in which cell nests are certainly present, but which are wanting in those features which characterise the greater number of tumours. We describe these tumours with Jadassohn as *organ nævi*. According to the preponderance of sebaceous glands, sweat glands, or of hairs, we speak of sebaceous, sweat gland, or hair nævi, etc.

The preparation represented in the figure is the type of a sweat gland nævus. The nævus nests (*n*) in the upper portion of the corium are markedly subordinate to the sebaceous glands (*t*). Nevertheless, the cell nests arranged in strings and columns are clearly observable; the cells are of the epithelial variety. In these aggregations of sweat glands a large number of acari (*a*) are to be seen. This acarus is certainly a harmless inhabitant of the sebaceous glands, and is in my experience exceedingly common both in the normal sebaceous gland and also in the sebaceous gland nævi, as well as in rhinophyma and all similar lesions. It is also found in the expressed sebaceous secretion, especially when this has been examined in oil and also in sections. In the latter case the acari are seated somewhat deeply, as is obvious from a glance at the figure, not in the duct of the sebaceous gland, but usually in the deeper portion of the acini. I find that they can be frequently stained in section with Benda's iron-hematoxylin method (cf. my *Dermato-histological Technique*, 3 ed., Berlin, Marcus, 1905, S. 45). Under a high power the oral orifice of the small worm-like acari can be made out; it is made up of a proboscis and three limbed feelers. According to Braun (*Die Tierischen Parasiten des Menschen*, 3 Aufl. Wurzburg, Stuber, 1903, S. 336), but few specimens are found in a single individual gland, and the Demodex folliculorum is present in 50 per cent. of adults, as also in children.

The preparation is taken from a boy of fifteen, in whom numerous symmetrical reddish nodules were present on the face, being specially marked in the naso-labial fold. The clinical diagnosis was that of "adenoma sebaceum."

Plate XVII. Fig. 39. **Condyloma acuminatum.**

× 330 Leitz, Obj. 6, Ocul. 2.

k = kariokinesis, c = overlapping granule, h = swollen cell, b = connective tissue, g = vessel, strc = stratum corneum, strg = stratum granulosum.

The condylomata, formerly erroneously described as papillomata, furnish the type of the acanthomata in which the size and proliferation of the

prickle cells in the form of numerous mitoses (k), among them multipolar cells being present, are excessively pronounced. To these characteristic features all others are entirely secondary, for the papillæ are involved in quite a subordinate manner, and, corresponding to the marked proliferation of the rete cells, are often extremely lengthened. As might well be anticipated, evidence of chronic inflammation rapidly supervenes in the connective tissue, for the origin of condylomata can frequently be traced to severe external irritation from pressure, &c.; these evidences are, as usual, the presence of dilated vessels and infiltration of leucocytes. Not only in this locality, but also in the rete, the plasma canals located between the swollen rete cells are forced asunder by numerous overlapping granules.

Keratohyalin is abundant, and the stratum corneum often displays a marked parakeratosis, *i.e.*, the nuclei of the epidermic cells persist. Hence the surface of the small tumour remains soft. This deficient hyperkeratosis, *i.e.*, the want of firm union between the epidermic cells which is responsible for this accumulation in heaps, causes, as pointed out by Unna, the absence of horny material which should hold together the papillæ, and on the other hand the absence of a firm horny layer which, by opposing a resistance, drives the epithelial aggregation directly downwards. In warty formations the most important feature is the hypertrophy of the stratum corneum; in condyloma accuminatum hypertrophy of the rete Malpighii.

According to the observation of Juliusberg, the epithelial covering of the papillæ as regards the most prominent elevations is in several points not so thick as on the lateral aspect of the upward-reaching tumour cones. At these points where the epithelium is defective a well-defined plug of leucocytes is found. In these circumscribed localities the resistance of the connective tissue at the points devoid of epithelium is abolished, and it is here especially that the unknown influence proceeding from the exterior exercises its prejudicial action.

Not merely the epithelium but also the connective tissue structure assumes a character wholly differing from that met with in warty growths. In condyloma the connective tissue is unusually soft and rich in juice; it is also abundantly furnished with blood-vessels and lymphatics, which are usually dilated. Hence, as the result of slight traumatism, at the site of the growth an escape of leucocytes occurs, and they not merely remain in the tissue but insinuate themselves into the interstices of the rete. They may sometimes be visible in very large numbers, and they display marked alterations of form, occasionally presenting no longer a round outline, but one drawn out and attenuated, and not seldom presenting tail-like appendages. A moderate number of mast cells is present in the cutis.

The characteristic features have been briefly and precisely summed up by Unna as follows :—There is a thin epidermic layer and absence of hyperkeratosis, the interspaces and the prickle cells are decidedly large, numerous and persistent mitoses occur in the upper portion of the prickle layer and complicated grooving of the surface; from the very commencement there is vesicular dilatation, which later leads to a chronic inflammation with escape of leucocytes and of abundant sero-fibrinous exudation, formation of new cells, and finally a persistent bifurcation of the papillæ through the epithelial hypertrophy.

Fig. 37. Naevus sebaceus.

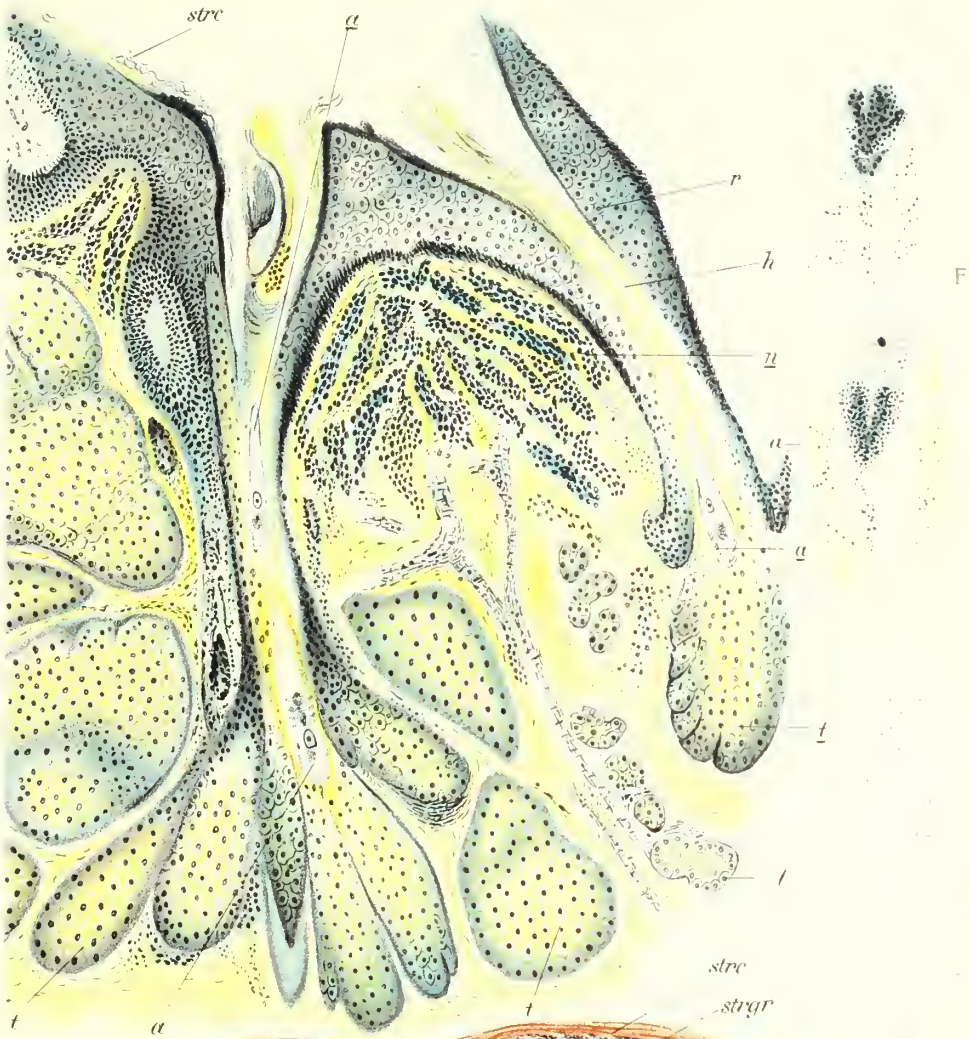


Fig. 38.

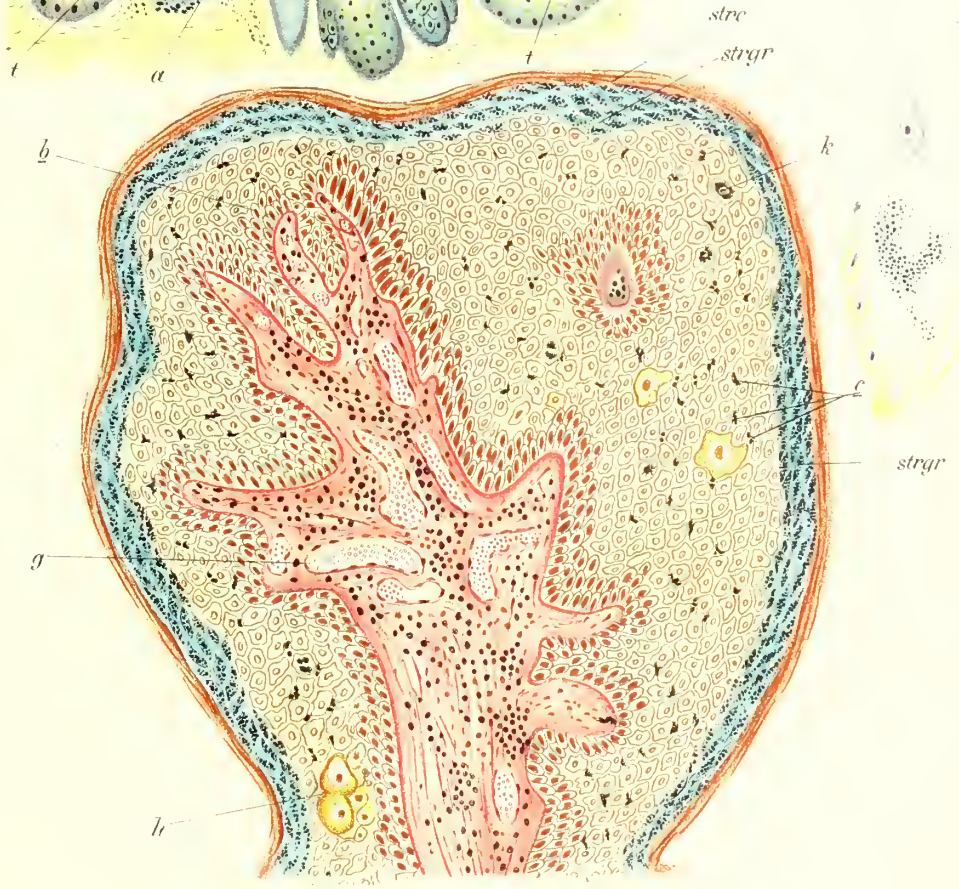


Fig. 39. Condyloma acuminatum.

Plate XVIII. Fig. 40. **Pemphigus foliaceus.**

× 105, Obj. 3, Ocul. 4.

r = rete, b = connective tissue, g = vessel, strc = stratum corneum, c = micrococci, bl = vesicle, e = eosinophile cell, d = endophlebitis, × Obj. 4, Ocul. 6, and a small portion of the bulla × 525, Obj. 7, Ocul. 3.

Histological examination in this malady does not throw any light on its severity and nature. For it might be assumed that, in the case of a disease so severe as pemphigus, the most important site for the nutrition of the epidermis, namely, the corium, would present marked changes. Yet this is not the case. For nothing more than a few dilated vessels and a trifling infiltration with leucocytes, in which mononuclear predominate over polynuclear cells, are found in the upper portions of the corium, while in the position of the subcutis merely marked vascular dilatation is present.

The tensely distended pemphigus bulla is acantholytic. From a study of the figure it becomes clear that the superior and inferior boundary layer of the bulla is formed of rete cells; and these, owing to the strong pressure of the exudation, are somewhat flattened out. It is obvious that a regeneration of the epidermis can be initiated from the floor of the bulla, which is in unbroken connection with persistent rete cells of the corium. Hence the pemphigus bulla does not leave a scar behind it because the germinal layers remain, and indeed form a portion of the floor of the bulla, while in the blister formed consecutively to a burn this is not the case. On the other hand, it is easy to understand that, occasionally and in special forms of pemphigus, regeneration of the epidermis takes place very rapidly before there is time for the formation of a new bulla to begin. In this way the new formed masses of epidermis and the bullæ become so intermingled that the whole gives the impression of puff paste. It is from this resemblance that the term pemphigus foliaceus is derived. The specimen figured is taken from a severe case of pemphigus. Two superimposed vesicles can be made out. The smaller, more deeply situated, displays the germinal layer occupying its floor, and upon it some layers of rete cells repose; the larger manifests a more pronounced covering of rete cells and a more abundant bulla content. This latter consists chiefly of red corpuscles with a few white, an evidence that, as a result of the strong *vis a tergo* consecutive to the general destruction induced by pemphigus, a marked diapedesis from the vessels of the corium into the rete vesicles has ensued. Finally, the intact bulla is not absolutely aseptic, and micrococci (*e*) penetrate it so soon as a breach of continuity occurs on the surface.

In some preparations I have discovered an endophlebitis obliterans, as is depicted in the figure (*d*, magnified 480). The lumen is markedly diminished in consequence of the formation of concentrically disposed layers of connective tissue; the endothelium is also proliferated. Should this latter condition be confirmed on further examination, it is clear that pemphigus must be classed with those maladies in which, as first pointed out by Philippson, hæmatogenous inflammation is usually localised in the veins, and thus pemphigus would be allied to those hæmotogenous infections to which Jadassohn (*Berl. Clin. Woch.*, 1904, 37) drew attention not long since.

We have found in our investigations, and chiefly in the earliest stages of the disease, indeed, in the first few days, a series of eosinophile cells which are

recognisable when magnified 800. It is worthy of notice that we have met with them in large quantities only in the earliest stages of pemphigus foliaceus and vulgaris. At a later period they are far less abundant.

Plate XVIII. Fig. 41. **Tuberculosis verrucosa cutis.**

× 85, Obj. 3, Ocul. 3.

h = epidermic proliferation, ri = giant cells, b = connective tissue, i = infiltration, r = rete, strc = stratum corneum, strg = stratum granulosum.

It follows from the prominent, warty-looking character of the growth that, histologically, there must be more especially a hypertrophy of the stratum corneum. These horny strata present a marked lamellary arrangement, and even in their uppermost layer they have preserved the staining quality of their nuclei. Along with this there goes an increase of the stratum granulosum, and the large number of keratohyalin fragments is very evident. Further, the cells of the rete Malpighii are much increased, and numerous mononuclear leucocytes are present in the inter-cellular spaces.

But all these are secondary features, and they sharply differentiate the chief characteristics of this disease from similar processes, *e.g.* a warty growth, by the presence in the corium of miliary tubercles which are met with more or less abundantly. In the markedly lengthened papillæ of the cutis, separated from the acanthotic rete cones, the characteristic giant cells are found in the stratum vasculosum sub-papillare.

The structure of these tubercles is altogether a typical one. Amongst the diseased areas are found one or more giant cells with a large number of peripherally distributed nuclei, and the centre of the tubercle is the seat of a coagulation necrosis (Weigert). In this region it is but rarely possible to detect the presence of tubercle bacilli. Tuberculosis verrucosa is manifested under the form of a mixed infection of tubercle bacilli and staphylococci, and the pustulation which is the regular accompaniment of the disease is rightly attributed by Riehl to a secondary infection due to a penetration from outside of the pyogenic micro-organisms.

A large number of plasma cells are, as in lupus, found in the vicinity of the giant cells; these plasma cells are recognisable by their eccentrically disposed nucleus, and the blue-coloured granules in the cell protoplasm, which are rendered very evident by their affinity for polychrome methylene blue. Mast cells are very few in number; they are detected by the violet-stained granules and their central nucleus, which is very susceptible to the methylene blue stain.

The whole turbercle acts as a foreign body, and gives rise to a genuine secondary infiltration of leucocytes in its neighbourhood. Karg surmises that to this thick wall appertains the function of carrying on the combat with the micro-organisms which have gained access, and of rendering them harmless. In this way, according to Karg, may be explained the local limitation of the malady for many years.

Nobl rightly lays stress on the excessive atypical proliferation of the outer germinal layer in combination with the specific alteration in the cutis layer, without any special change in the reticulated connective tissue. In lupus verrucosus, on the other hand, the involvement of the epithelial layer is quite secondary. The chief alterations are here comprised in the area of the collagenous connective tissue.

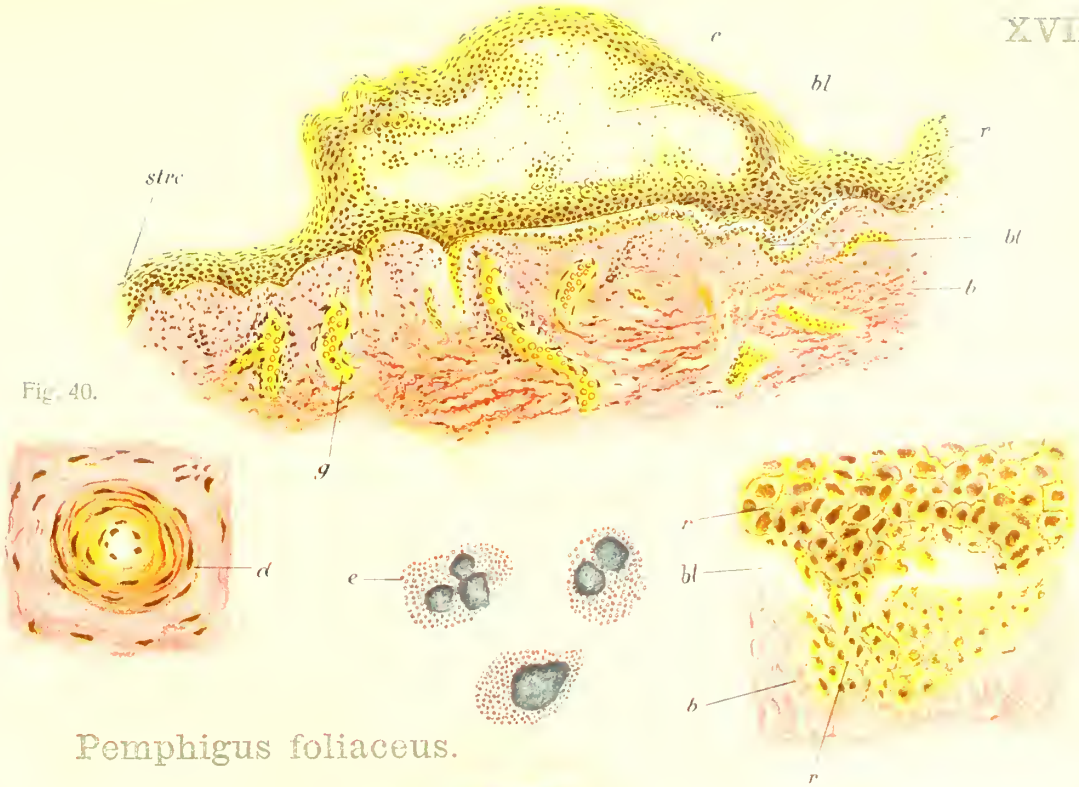


Fig. 40.

Pemphigus foliaceus.

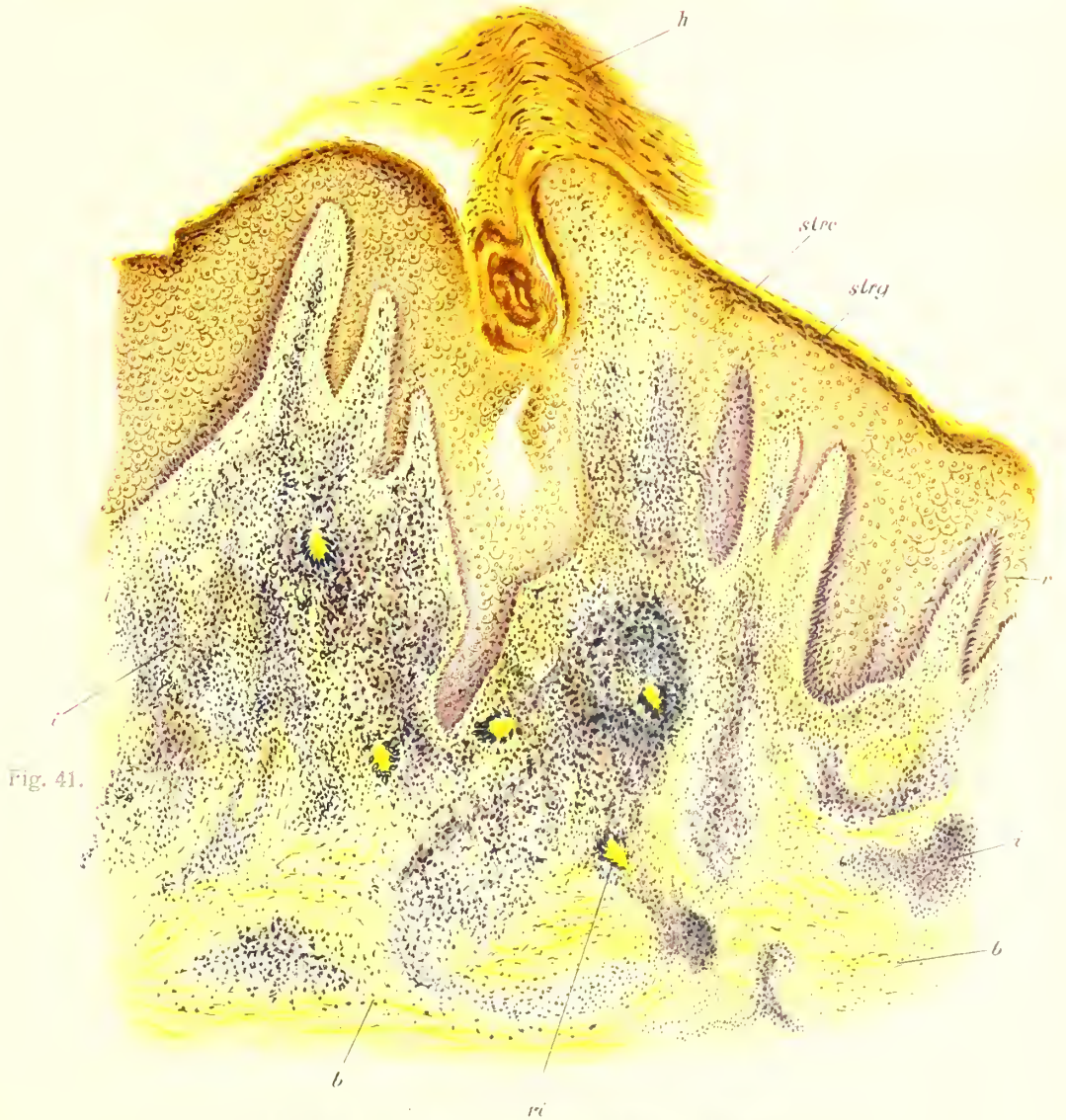


Fig. 41.

Tuberculosis verrucosa cutis.

Plate XIX. Fig. 42. **Psoriasis vulgaris.**

× 85, Obj. 3, Ocul. 3.

p = parakeratosis, i = infiltration, strc = stratum corneum, r = rete, b = connective tissue, g = vessel.

In psoriasis we return to the type of parakeratosis. In the first place, we find in the corium dilated blood-vessels and lymphatics, and in their vicinity collections of mononuclear leucocytes.

As result, an abnormal formation of horny matter, together with an increased production of epidermic scales, ensues, with œdema of the superimposed epithelium. The keratohyalin of the stratum granulosum and the eleidin of the basal epidermis have altogether disappeared. On the other hand, the nuclei of the horny cells are well maintained for the most part, and between nucleus and horny membrane a large mass of colour-absorbing remains of the protoplasm is discernible. In spite of the fact that the characteristic scales of psoriasis are of horny nature, yet their investing mantle resists the digestive action of hydrochloric acid and pepsin. It is clear that there is here merely a prolonged and simple process of cornification without formation of keratohyalin and disappearance of nucleus. In consequence of this imperfect formation of horny matter the individual layers remain united, and large collections of cells are formed which are clinically described as scales, inasmuch as a marked horny change is prevented through abnormal soaking of the epithelium : parenchymatous œdema. At a later period the rete becomes markedly hypertrophied, and the widened inter-papillary rete cones are especially characteristic. The supra-papillary prickle layer is much thinned, and to this thinning is attributed the slight bleeding which occurs when the psoriasis scales are removed by scratching. As a result of the antecedent abnormal cornification, a pronounced overgrowth of epithelium occurs in which many air-containing chinks and spaces are met with. To this cause is assigned the shining appearance of the scales.

Between the layers of scales a quantity of leucocytes are collected in the form of striated aggregations. According to Kromayer (*Arch. f. Dermat. u. Syph.*, 1890), the number of these wandering cells preserves a direct proportion to the intensity of the psoriatic process.

Munro (*Annal. de Dermat. et de Syph.*, 1898) holds that a slight erosion is present on the surface of the epidermis. This erosion is filled with leucocytes, and hence the very earliest stage of psoriasis is characterised by the occurrence of a miliary abscess in the epidermis. But Burgener points out (*Dtsch. Medizinal Ztg.*, 1903) very justly that these abscesses are absent in pure eruptions of psoriasis developing under the protection of thicker epidermis. Hence it would seem to be impossible to attribute to this cause a predominant influence in the development of the psoriasis eruption.

Plate XIX. Fig. 43. **Pemphigus vegetans.**

× 85, Obj. 3, Ocul. 3.

a = abscess due to staphylococci in the epidermis and rete, b = vesicle, bl = bulla partly filled with epidermic and partly with rete cells, i = infiltration, r = rete, m = mast cells, i = infiltration, g = vessel, b = connective tissue, strc = stratum corneum, strg = stratum granulosum.

Corresponding to the clinical course of the malady, the acanthotic new growth preponderates in the histological aspect of the disease. Not only are the rete cells increased in number, but they are enlarged to several times the normal and also frequently manifest a vacuolar degeneration. Karyolysis and karyorexis, as also chromatolysis, are frequently observed, as was specially pointed out by Stanziale (*Annal. de Dermat. et de Syph.*, 4 *série Bd.* 5), but karyokinesis is rare and for the most part atypical.

Within not only the rete but also the epidermis vesicles or, rather, abscesses make their appearance; these are filled partly with epidermic cells, partly with rete cells, together with leucocytes and staphylococci. In some vesicles eosinophiles are also detectable, as pointed out by Karl Bernhardt (*Inaug. Diss.*, Freiburg, 1892). This double stratification on the part of the vesicle has been specially emphasised by Weidenfeld (*Arch. f. Dermat. u. Syph.* 67 Bd. 1903, S. 920):— "The stratum corneum is elevated and the rete is divided in many cases so that in certain localities it appears to be torn. The contents of the little vesicle covered by the stratum corneum completely correspond to the contents of the several divisions of the compartments, so that it does not seem unjustifiable to regard the spaces in the lattice work as being abortive vesicles which, through tears in their structure, frequently become united with the uppermost vesicle. Hence we arrive at a sort of laminated vesicle."

Contrary to what happens as regards the proliferation, the hyperkeratosis recedes. Yet it is well maintained in some points, and here also keratohyalin is well developed.

A marked dilatation of vessels ensues at an earlier stage in the papillary layer, and in the deep portion of the corium an endo-, meso- and peri-arteritis or phlebitis ensues. Hamburger and Ruhel (*The Johns Hopkins Hospital Bulletin*, March, 1903) found a marked infiltration of leucocytes in the vicinity of the vessels. Weidenfelt distinguished a stage of vesicle formation in pemphigus vegetans, in which the vesicles are not dilated; and a stage of intra-bullous vegetation, in which the vesicles are moderately dilated; and lastly a stage of vegetation in which the vessels are dilated to the maximum.

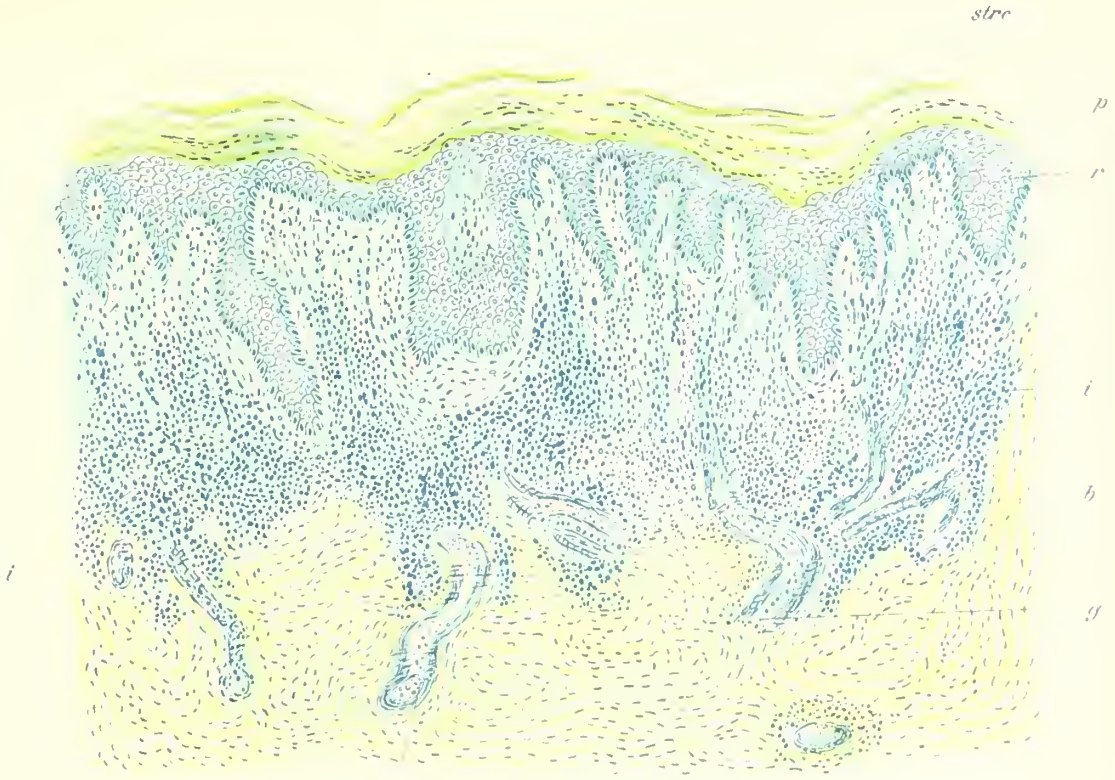


Fig. 42. *g* Psoriasis vulgaris.

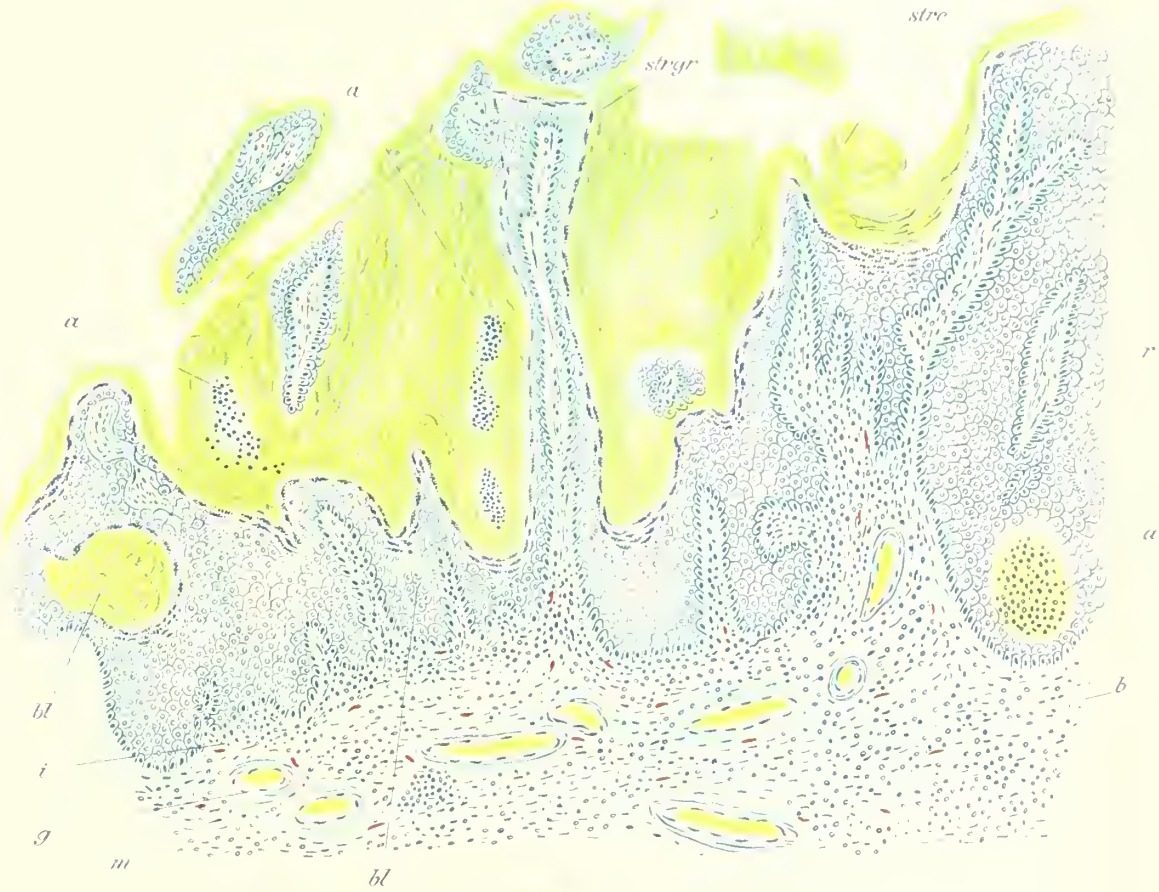


Fig. 43. Pemphigus vegetans.

Plate XX. Figs. 44, 45. **Psorospermosis follicularis vegetans.**

× 85, Obj. 3, Ocul. 3.

r = rete, b = connective tissue, f = keratohyalin, strc = stratum corneum, strg = stratum granulosum.

Darier's bodies (d) are exceptionally magnified 800 (Ocul. 3, Oil-immersion $\frac{1}{12}$).

The interest of this disease is bound up with the *corps ronds*, first described by Darier. These were for some time regarded as parasites, and the malady was then described as psorospermosis follicularis vegetans. Clinically, the horny masses project from the follicle, and this is evident in the figure where a low power has been employed. The figure displays a follicle filled with a hard, horny mass which spreads over the surface; from the strict histological standpoint, the figure would thus depict keratoma follicularis vegetans. Within, or at the edge of these horny masses, approaching the stratum granulosum, a large number of peculiar brightly shining cells, which are quite unusual within the epidermis, are observed; these cells are of large size; they possess a bright protoplasm and a dark nucleus. With picrocarmine staining they stand out prominently from the non-nucleated horny cells, as in the specimen here represented. Their most marked resemblance is to the rete cells which, under the influence of the most diverse anatomical processes, *e.g.* not seldom through the acanthotic process, become dropsically swollen to inflamed and infiltrated warts. At the first glance these bodies of Darier would be regarded as vacuolated or dropsical rete cells, but topographically they occupy an entirely different situation from that of these cells, *viz.*, the epidermis. It seems to me that in some measure a retardation of the developmental process has preceded this pathological change.

Probably the following antecedent process has taken place. In the normal condition from the rete cell, a cell of the stratum granulosum is derived, and the latter species of cell makes use of this opportunity to acquire keratohyalin. Gradually it is converted into a horny cell.

In the dermatosis of Darier now under discussion, not only is this process interrupted, but it occurs in a retrograde sense. The keratohyalin-containing cells of the stratum granulosum undergo once again a retrograde metamorphosis, and in doing so they, through the influence of an unknown agent, do not form normal cells but the *corps ronds*. The absolute resemblance of both classes, of

normal rete cells and of the *corps ronds*, is evident when both low and high powers are made use of: the rete cells retain their normal crenation, but the *corps ronds* do not display this character.

But that these bodies are psorosperms there is not the least evidence available; this theory has been universally abandoned, and the *corps ronds* are now regarded as special forms of cell degeneration.

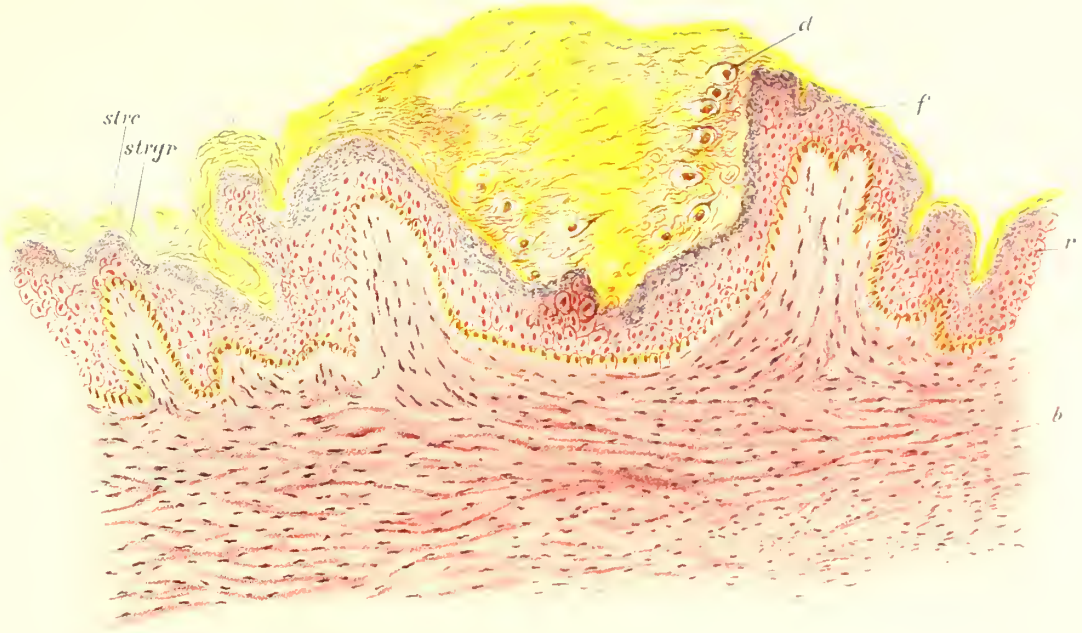


Fig. 14.

Psorospermosis follicularis vegetans.

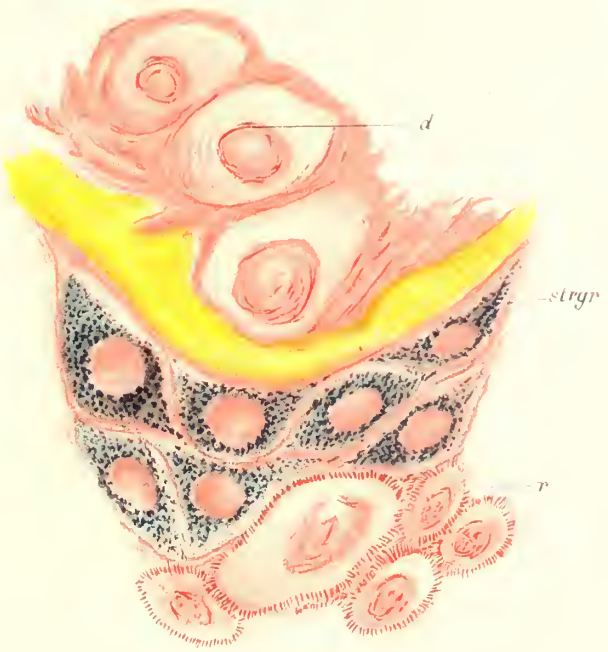


Fig. 15.

Plate XXI. Fig. 46. **Sarcoma cutis.**

× 85, Obj. 3, Ocul. 3.

k = lime, sarcoma cells, strc = stratum corneum, r = rete, b = connective tissue, g = vessel.

The case from which the section illustrated was prepared was that of a woman of 45, who suffered from an isolated sarcoma of the left leg, but who was in other respects healthy, except for the presence of arterial degeneration.

In the locality referred to a well-defined collection of cells was present, replacing the autochthonous tissue. The sarcomatous tumour was composed of round cells, having a polymorphous nucleus, intermixed with spindle cells which had originated through inflammation from the original connective tissue. A certain amount of reticular substance can be seen lying between the sarcoma cells, and this distinguishes the growth from carcinoma.

It is particularly important to emphasise the fact that in this instance, as usually happens in sarcoma, the elastic tissue is entirely destroyed, and mast and plasma cells are wanting; this is not the case as regards tumours and other inflammatory processes invading the skin. Further, a weighty criterion between this and other tumours, *e.g.* mycosis fungoides, is that the majority of sarcomata only attack the papillary layer at a late stage. The latter, and a superficial layer of the cutis, generally remain free from the special sarcomatous tissue growth.

A peculiar feature of the present case is the occurrence of calcareous deposit in the tumour. On the addition of hydrochloric acid the deposit dissolves. The calcification has extended from the lymphatics in a similar manner to that described by Perthes as occurring in endotheliomata which have undergone calcareous degeneration.

Plate XXI. Fig. 47. **Sarcoma melanoticum.**

× 85, Obj. 3, Ocul. 3.

r = rete, strc = stratum corneum, b = connective tissue, g = vessel, s = sarcoma cell, i = infiltration, p = pigment cell; the latter is × 525, Obj. 7, Ocul. 3.

The sarcomatous growth here represented originated in a nævus. A moderately abundant intercellular substance lies between the spindle-shaped sarcoma cells. The infiltration (i) should be taken note of as being an evidence of the inflammatory changes which probably preceded by some time the appearance of the malignant new formation. The very special malignancy of this

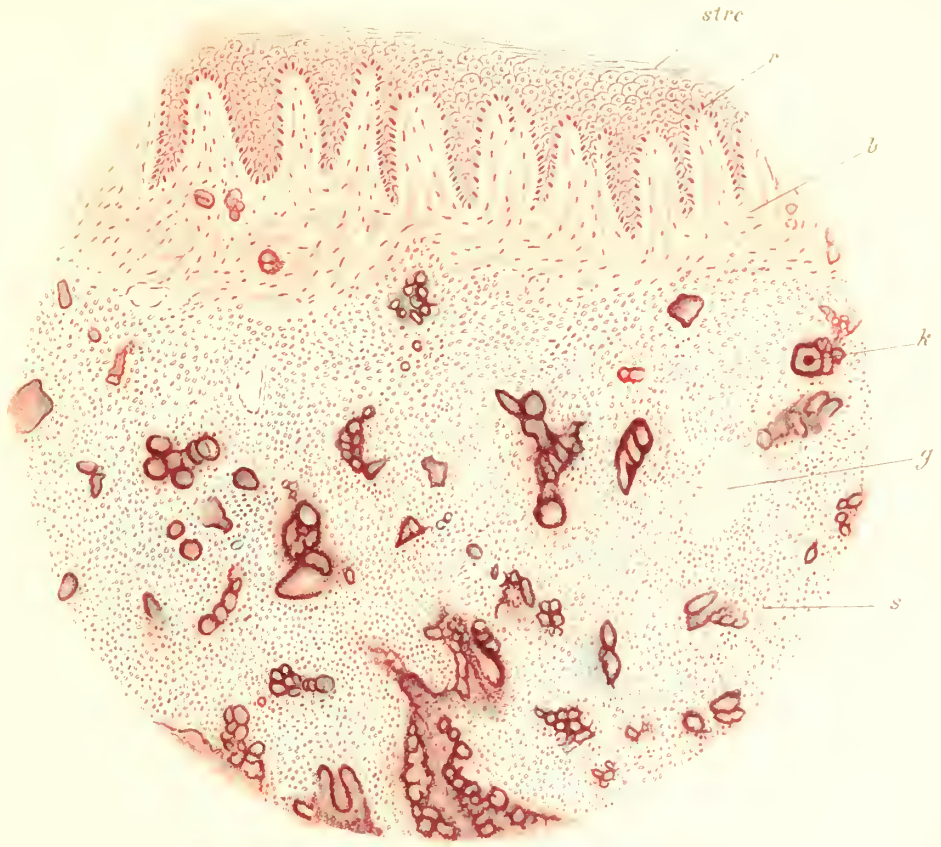
form of sarcoma is evidenced by the presence of very large and widely-ramified pigment cells (p), which are clearly visible under a higher power.

In this tumour, which has taken its origin in a pigmented nævus, the pigment has certainly been deposited for some time in the cutis. The pigment penetrates between the bundles of connective tissue of the autochthonous structure into the tumour, and then the hitherto latent energy of the quiescent cells is aroused to activity, just as I have described in a case of nævo-carcinoma in *Festschrift für J. Neumann* (Vienna, 1900). These bundles send long, slender outgrowths in all directions between the tumour cells, and the pigment, hitherto united in ball-like masses, becomes progressively resolved into delicate granules.

This case may be classified with that of Ribbert (Ziegler's *Beitr. z. path. Anat. u. z. allg. Path.*, 21, 1897) as one of chromatophorous melanoma. Ribbert considers this cutaneous melanoma to be a specific form of tumour, in the sense that it is made up of elements which originate in a special form of cell, *i.e.* chromatophores.

Just as I am convinced of the accuracy of Unna's view that carcinoma may take origin in nævi, so I must emphasise and support the general accuracy of the view that occasionally melano-sarcoma may originate in nævi. I have already enunciated this opinion, and it is supported by the present case, and the writings of Bauer (Virch. *Arch.* 142), Green (Virch. *Arch.* 134), Henson and Nölke (*Dtsch. Arch. f. Klin. Med.* 62, 1899), as well as of Wiener (Ziegler's *Beitr. z. pathol. Anat. u. z. allg. Path.*, 25), leave no sort of doubt that nævo-sarcoma may occur as well as nævo-carcinoma. Here the pigment cells lie in the stroma, while in melanotic carcinoma the alveoli are most abundantly filled with pigment-containing cells.

Fig. 16. Sarcoma cutis.



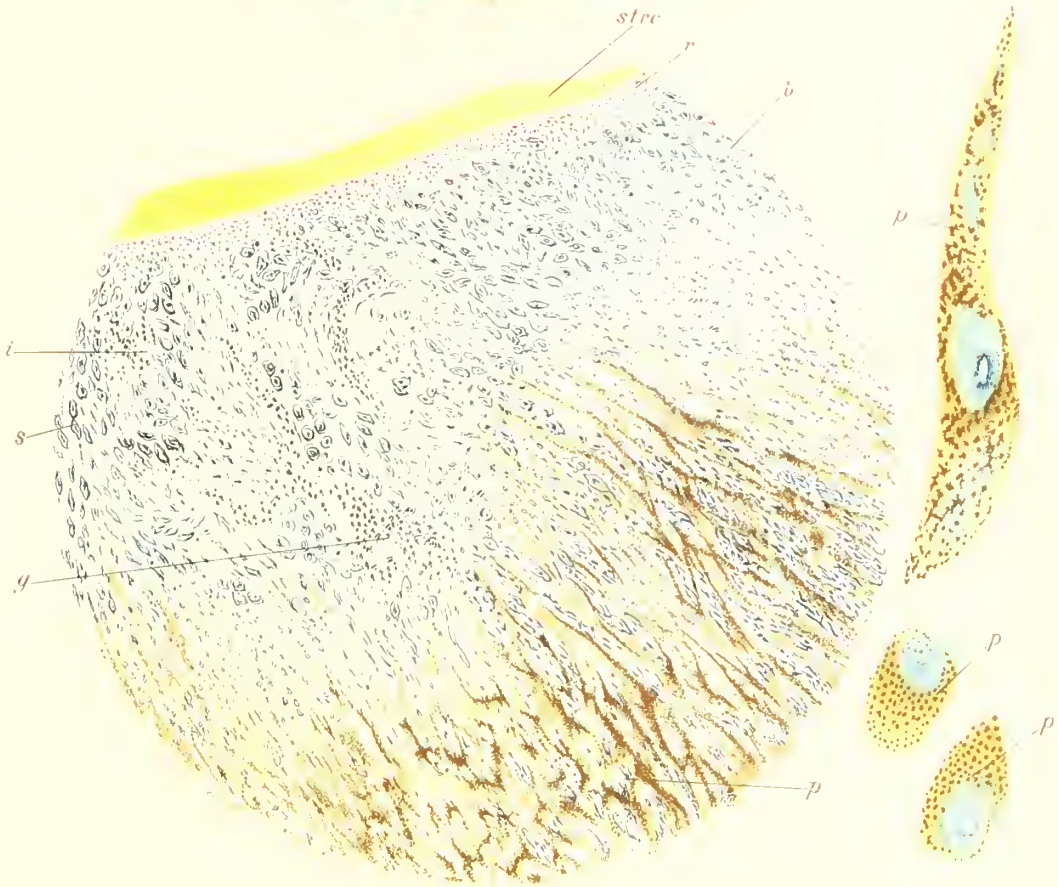


Fig. 17. Sarcoma melanoticum.

Plate XXII. Fig. 48. **Scleroderma circumscriptum.**

× 85 Leitz, Obj. 3, Ocul. 3.

strc = stratum corneum, e = elastic fibre system, r = rete, g = vessel, s = sweat glands, f = fatty tissue, b = connective tissue.

It has always been to me a matter of surprise that, in the atrophic stage of scleroderma, whilst the connective tissue, the hairs, and the sebaceous glands are atrophied, the elastic fibre system appears to be hypertrophied. But it is possible that this increase of the elastic fibres should be regarded as relative only, for in consequence of the disappearance of the connective tissue the elastic fibres become confined in a small space. Still, it is not inconceivable that here there may be a new formation of elastic fibres. For it is a striking feature, both as regards arteries and veins, that a considerable increase of the elastic tissue elements has been observed. Indeed, this increase is so marked that it is no longer possible to recognise the details of the course and arrangement of the vessels. The membrana elastica is disposed in almost four times the thickness of layers as it is in the normal condition, this being the result of its exuberant development. Of the fibrillary connective tissue but little can be made out.

The strikingly small number of connective tissue cells and the defective development of the fibrils point still more strongly to a marked diminution of tissue, as the latter only rarely presents juice clefts and manifests an almost homogeneous appearance. This is particularly noticeable, and does not support the view of Unna, who lays weight, as a prominent characteristic of all the histologically differentiated sub-varieties of scleroderma, on the occurrence of hypertrophy of the collagenous inter-cellular substance.

In consequence of the atrophy, in the same way as a scar, the epithelium encroaches in a straight line on the underlying tissue. Only the sweat glands remain in their original condition.

Plate XXII. Fig. 49. **Tricho-epithelioma papulosum multiplex.**

× 105 Leitz, Obj. 3, Ocul. 4.

l = lymph space, w = growth, h = hair and hair sheaths, b = connective tissue with nuclei, g = vessel, r = rete, strc = stratum corneum.

The figure is reproduced from a preparation which I owe to the courtesy of my friend and former pupil, Professor Dohi, of Tokio.

In the corium many epithelial aggregations are observed; these are separated from the epithelium by normal connective tissue. As also in the case of Jarisch (*Arch. f. Dermat. u. Syph.*, 28, 1904, S. 186), these collections are made up in

part of round cells, in part of ramified nodular cell elements, usually attaining a middle region, which generally encloses a hair. In other localities the epithelial strings and round epithelial accumulations, through central partly colloid part corneous degeneration, assume a glandular or cystic form. As a rule, the external root sheaths are the starting points. Just as in Jarisch's case, the connection of the cell elements with the hair follicles was easily demonstrated. "It is not unusual to see transverse sections of hairs lying within a ramified, nodular, interconnected mass, suggesting the horn of a deer." I entertain no sort of doubt that in this case, as in that of Jarisch, the epithelioma originates in the hair follicles of the (lanugo) hairs which occur in the club-formed stage, and from the upper and middle third of the same. Hence, I consider it correct to adopt the terminology of Jarisch, who employs the expression tricho-epithelioma papulosum multiplex, instead of making use of the term epithelioma (Brooke, Wolters), or acanthoma (Unna) adenoides cysticum.

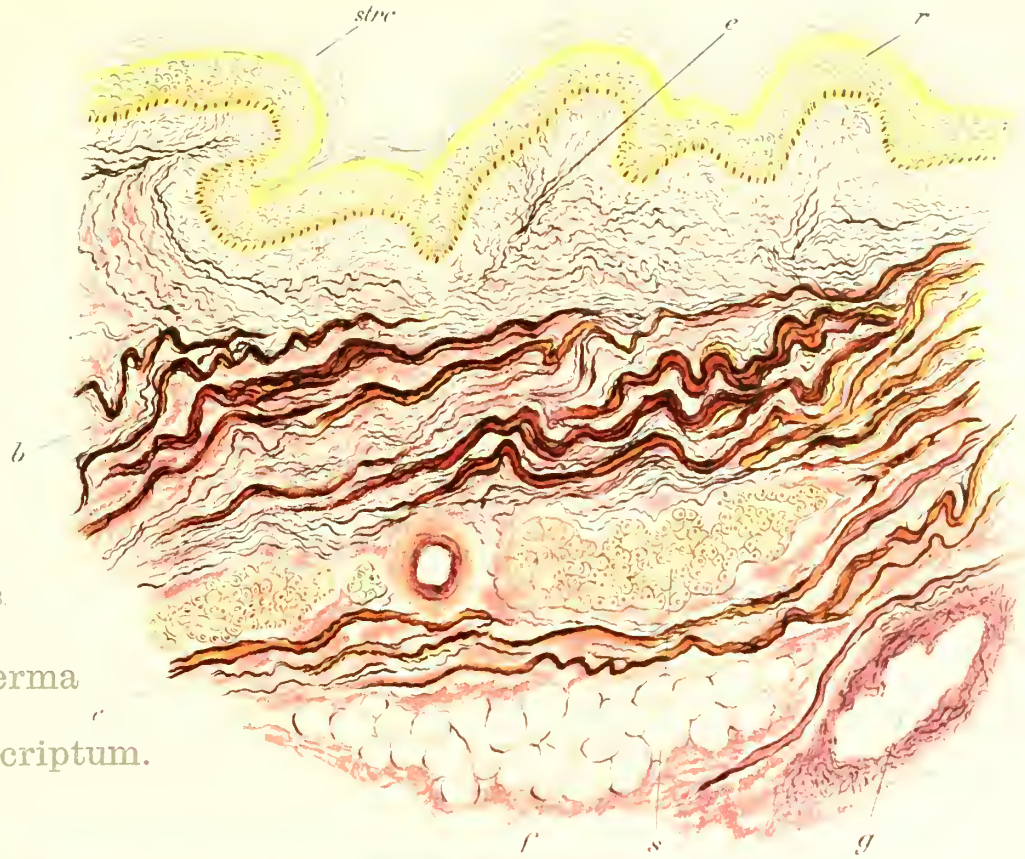


Fig. 48.

Scleroderma circumscriptum.

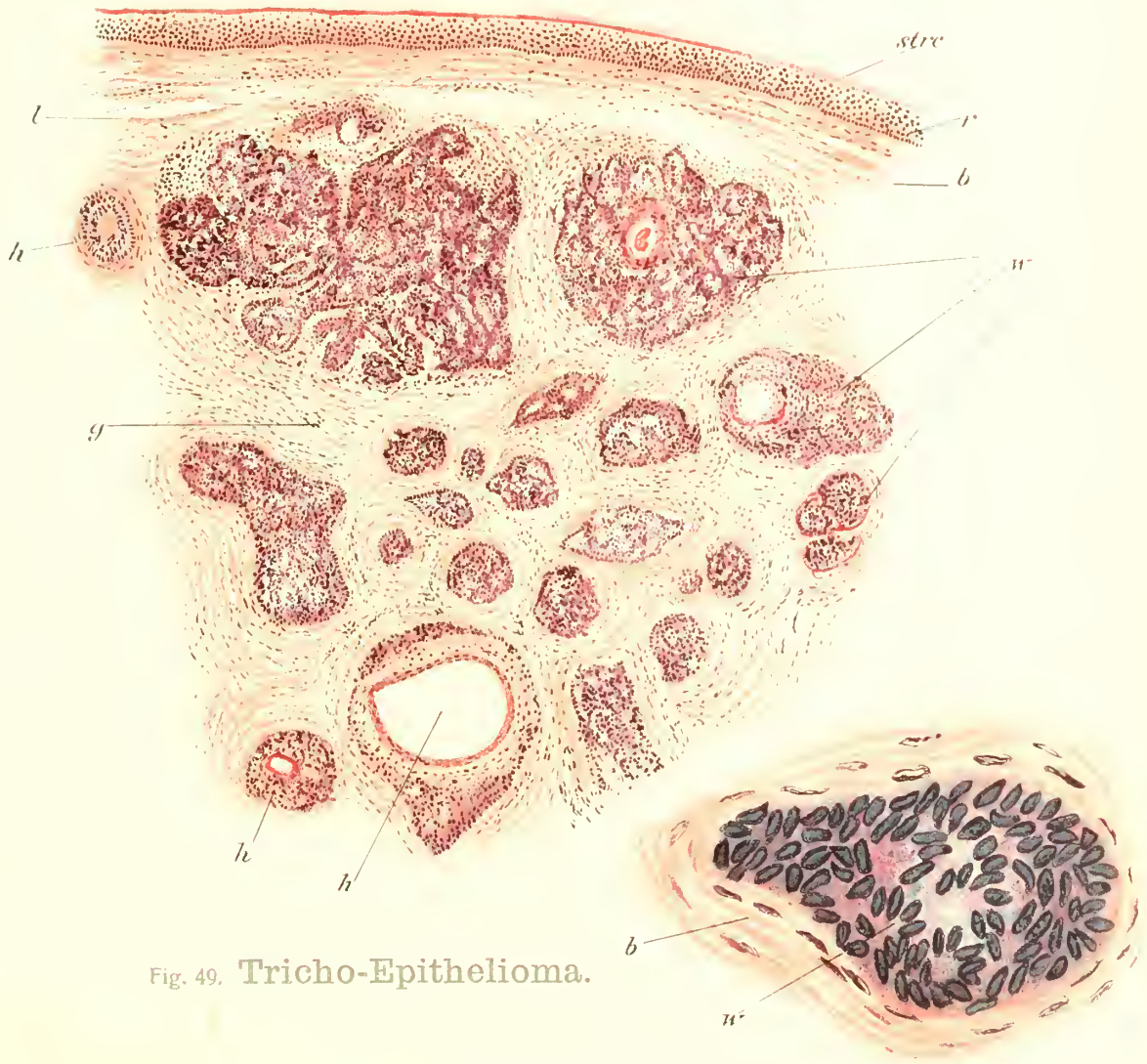


Fig. 49. Tricho-Epithelioma.

Plate XXIII. Fig. 50. **Ulcus durum.**

× 85, Obj. 3, Ocul. 3.

ri = giant cells, g = vessel, p = periadventitial infiltration, i = infiltration, r = rete, strc = stratum corneum, strg = stratum granulosum.

In contrast to the deeply eroding soft chancre, the superficial character of the ulcerative process of primary syphilis is very striking. Further, the transition from sound to diseased tissue is very abrupt. The whole structure, as far as the upper layers of the cutis, is the seat of an extremely abundant cell infiltration of the granulation tissue type. These cells have taken origin in escaped leucocytes, inasmuch as they are found surrounding the vessels. But under the influence of the syphilitic virus there is an extremely rapid development, as Neisser has proved, of elongated, compressed spindle cells, possessing a small nucleus and relatively abundant protoplasm. Larger epithelioid or mast cells are present in smaller numbers; these latter are especially marked at the periphery. Exceptionally, a number of giant cells are observed, as in the section now under discussion. These giant cells are of polygonal outline, and contain a large number of granules, which are located at the periphery and arranged in wreath form. There is superadded a free formation of new vessels and an endarteritis obliterans, which is a result of thickening of the walls and proliferation of the endothelium and the adventitia. The vessels are stiff and thickened, and the lesion leads to a diminution in their calibre, and sometimes to obliteration of their lumen.

According to Unna, this lesion is the result of penetration of certain points of the vascular wall by round cells from the exterior; it may be that they gain access from the outside, or else originate locally, and in this way give rise to concentric diminution of the vascular lumen. As a rule, the endothelium takes part in the process. Rieder considers that the vessels which are most deeply involved are not the arteries, but the veins and lymphatics.

Neisser looks upon a hyperplastic process involving the formed connective tissue cells as being especially characteristic; this process can be clearly recognised beneath the induration. There are observed in this case a number of large, thick, granular cell elements furnished with prominent nuclei. The quite insignificant mitosis offers a very marked contrast to this very pronounced involvement of the connective tissue cells (V. Marschalko). Krzysztalowicz noticed the occurrence in the infiltration of cells varying in type and size, with much spongio-plasma and but little granulo-plasma: spongioblasts which were joined together by processes and formed an anastomosis in the meshes of which plasma cells were observed.

The nature of the initial sclerosis depends, according to Ehrmann, upon the extent of the lymphatic system which is contained in the infiltration. At the periphery of the sclerosis the blood-vessels are greatly increased in number, but in the area of the erosion their number is diminished. Hence there ensues upon a completely bloodless zone another whose capillaries are remarkably dilated which is filled by the arterial pressure, but which no longer lends itself to an afflux of blood. Hence also it follows that the initial sclerosis, on the smallest attempt to bend it, will become anæmic at the locality dealt with.

Essentially there occurs, contrary to what holds in soft ulceration with its destruction of infiltration products, in the primary lesion of syphilis, a conversion of granulation tissue into connective tissue. Spindle cells, vascular changes, and hyperplastic tissue cells are met with. More especially as regards the vessels it is a question of productive rather than of inflammatory exudative early phenomena.

Plate XXIII. Fig. 51. **Dermatitis papillaris capillitii.**

× 85, Obj. 3, Ocul. 3.

strc = stratum corneum, strg = stratum granulosum, r = rete, m = mast cells, p = pigment cells, pl = plasma cells. The last three varieties of cells are × 800 (Ocul. 3, Oil-immersion $\frac{1}{12}$). b = connective tissue, g = vessel, s = sweat glands, h = hair, pa = papillary layer.

In direct proportion to the definiteness and stability of the clinical picture in this disease, so is the anatomy of the same uncertain and imperfectly worked out.

The figure represents the appearance in a typical case, that of a man of 26 in whom the lesion occurred in the neck. A portion was removed from the centre of the tumour. It is obvious that the stratum corneum is markedly diminished, and is formed merely by a layer of granule cells, while the rete is hypertrophied and acanthotic. Between the acanthotic rete cells the cross sections of the œdematous papillæ stand out as bright spaces from the rete cells. The most important change and that which is most striking is the plasmoma formation in the corium; here are observed large masses of plasma cells, and between them are mast, with many pigmented, cells.

The plasma cells are distributed in large masses between the atrophied hairs. More particularly with a higher power are conspicuously seen the quadrangular polygonal or irregularly shaped plasma cells with their eccentric nucleus and blue granulations, which with the metachromatic method of staining with methylene blue are clearly distinguished from the tail-shaped lengthened mast cells with their central blue nucleus and violet granulations. Between them cells stuffed with pigment are located, which are the more remarkable inasmuch as, clinically, no hyper-pigmentation is recognisable.

The fully developed stage of the malady has now been described. But it is not surprising that different observers have obtained results with no resemblance to each other when studying different phases of the disease. Thus, *e.g.*, I find in the excellent atlas of Dockrell (Longmans, Green & Co., London, 1905) at plate 31, a drawing which obviously portrays the early stage only of the lesion. In this plate there is no indication of excessive plasma formation such as is depicted in the present instance. The early stage is here, as it is in the development of urticaria pigmentosa, as we have already seen. In urticaria pigmentosa, when fully developed, we have to do with a very strongly pronounced mast cell tumour. If this is still regarded by many observers as doubtful, the hesitation is due to the fact of their having studied the early stage, but not the fully developed process. It is precisely the same as regards the maximum stage of the large plasma cell tumour in dermatitis papillaris capillitii. I am here entirely at one with Guszman (*Dermat. Zeitschr.* Bd. XII), who emphasises the presence of plasma cells in large numbers at the acme of the cell infiltration.

In comparison with this accumulation of innumerable plasma cells, the other morbid changes occupy an entirely subordinate position.

Hence it is manifest how very incorrect from the histological standpoint is the use of the term acne-keloid. It may, indeed, be allowed that from the clinical point of view the use of this term may be justified, for from the clinical side it certainly appears that a scar with secondary connective tissue formation may originate from a folliculitis. But if it is held that, in keloid, a fibroma of the skin free from elastin is under observation, then the new connective tissue formation in acne-keloid occupies a secondary position, and is altogether eclipsed by the plasmoma overgrowth. The elastic fibres are quite unaltered.

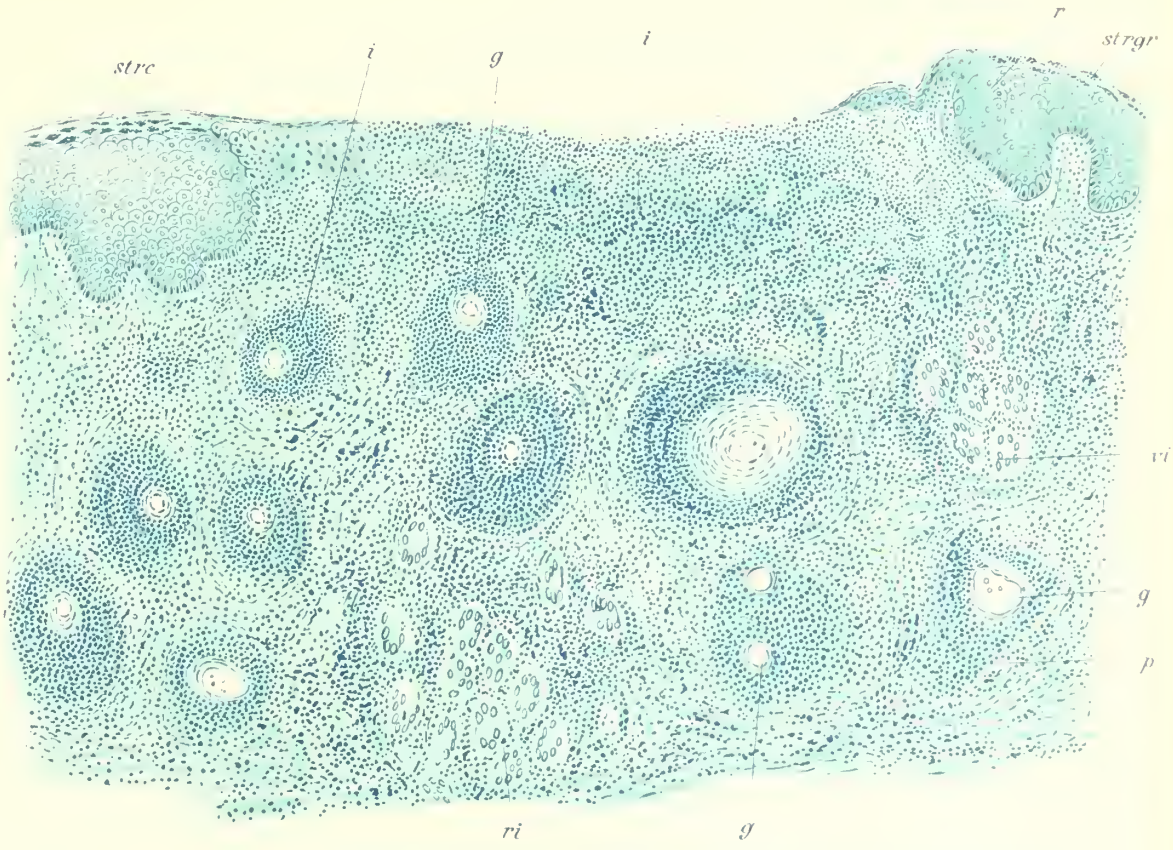


Fig. 50. Ulcus durum.

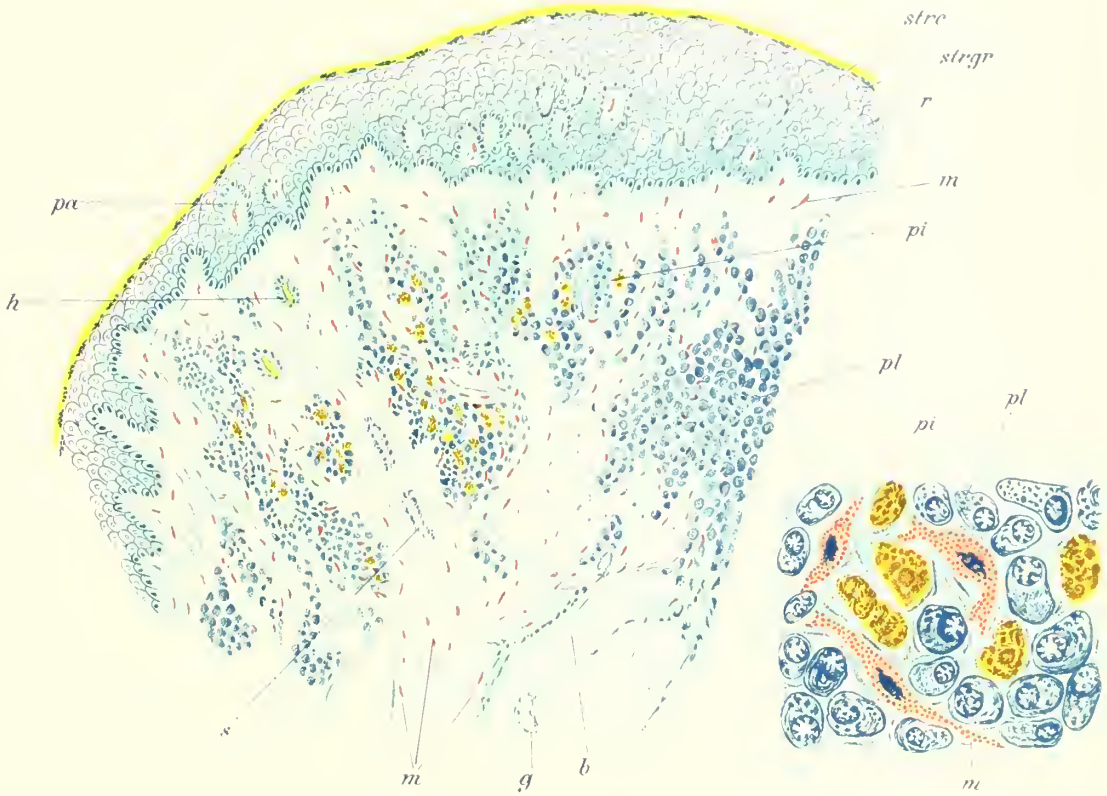


Fig. 51. Dermatitis papillaris capillitii.

Plate XXIV. Fig. 52. **Verruca vulgaris.**

× 47, Obj. 2, Ocul. 3.

p = papillae, g = vessel, s = sweat gland, e = eleidin, strg = stratum granulosum, hd = dropsical cells; the latter are × 300 (Obj. 6, Ocul. 3), strc = stratum corneum.

Warts are divided into two classes, the hard and the soft. The histological type of keratoid or acanthoid growth depends upon whether the proliferation of the stratum corneum (keratoid) or the increase of the prickle cells (acanthoid) predominates. The specimen figured is taken from a hard wart of the hand. The non-nucleated cells of the stratum corneum are proliferated to a very decided extent, and arranged in layers like tiles. Eleidin is present in the proximal portion in the form of oily masses, which are collected together in the lowest strata of the epidermis, and are particularly well displayed when picro-carmine staining is made use of. Under these circumstances the greater portion of the epidermis is distinguished from the cells containing eleidin, which are stained red, by its yellow colour. But at the point of transition to the rete Malpighii the stratum granulosum displays a moderately pronounced proliferation and marked accumulation of keratohyalin, which almost completely fills the cells in the form of blue hemotoxylin-stained small masses. Then follows the somewhat thickened but, in comparison with the stratum corneum, less hypertrophied, rete Malpighii, whilst between the proliferated rete cones the delicate papillæ stand prominently forth.

In the rete more particularly are observed numerous vacuolated cells, in which the accumulation of increased nourishment with lymph has led to distension of the periphery of the cell and to vesicle formation (vacuolar degeneration).

The papillary layer is not proliferated and is in all important respects normal; only in a few points are the capillaries dilated, and in these same localities inflammatory infiltration is present; the infiltration is made up chiefly of mononuclear leucocytes. But occasionally, and probably in consequence of external irritation, the inflammatory process in the corium is very pronounced, and then some small overlapping nuclei are present even in the rete layer. The deeper layers of the corium are quite normal. It follows from the arrangement of the structures of the hand that a certain number of sweat glands will be observed in the lesion.

Plate XXIV. Fig. 53. **Xanthoma.**

× 135, Leitz, Obj. 3, Ocul. 4.

ri = giant cells, x = xanthoma cells, both are × 625, Leitz, Obj. 7, Ocul. 4, b = connective tissue, bi = nucleated connective tissue cells, i = infiltration, r = rete, g = vessels, strc = stratum corneum, strg = stratum granulosum.

The xanthoma infiltration is seen lying beneath the normal epidermis with usually a fairly well defined pigmented stratum cylindricum, and separated from the epidermis by a moderately wide normal corium. The xanthoma is made up

of a diffused conglomeration of peculiar fat-like masses, consisting in part of typical cells and in part of irregular but clearly defined aggregations. The healthy portion of the corium, that not attacked by the new formation, displays numerous pigment cells in the cutis, together with long rows of irregularly distributed mast cells and most obviously dilated lymphatics.

The morbid process would seem to commence in the vicinity of the vessels. It would appear that the adventitia sometimes becomes split into laminæ; here the earliest xanthomatous masses are developed. My own observations have led me to the conviction that these masses present, in the first instance, a genuine cell formation. Hence it is important to realise that in the early stages the presence of xanthoma cells must be recognised as an indispensable characteristic of the disease. Usually small cells furnished with one or more nuclei with a membrane of a fatty, honeycomb structure are met with. It is often possible to convince oneself that the connective tissue cells are distended with the xanthoma masses, and a large number of fine granules are detectable within these cells. The more chronic the process, so much the more do the typical features of the xanthoma cell disappear. The cells become more and more distended, some of them adhere together, and in this way an apparent giant cell is produced; it is quite usual to be able to trace the gradual crumbling away of the nuclei as a consequence of the xanthomatous infiltration.

Through gradual distension the cells finally rupture, and the interspaces of the connective tissue are filled with these xanthoma masses which no longer contain nuclei. And in the same way the lymph spaces are gradually filled up; these masses are developed in the contiguity of the small lymphatics, the capillaries, and above all the hairs. It is only natural to anticipate that in a purely mechanical manner the elastic fibres will be pushed asunder and rarefied. Thus it may happen in the case of chronic xanthoma that merely the completed and quiescent process may be observed. Then the whole field will be occupied by a large quantity of xanthoma masses, and the connective tissue fibres, very slightly developed, will be forced asunder by these masses. But while large aggregations have become welded together, the contour of the single cells is frequently entirely lost; these xanthoma cells are distended, then flattened, and then become united one with another. Under these circumstances merely a few elastic fibres are detectable within the whole of the lesion, just as Unna has described in masterly fashion (*Histopathologie der Hautkrankheiten*, Berlin, 1894, and *Mon. f. prakt. Dermat.* 26, 1898), the fragments are all that remain of the original structure.

Therefore we agree with Knauss (*Virch. Arc.* 116) when he defines xanthoma as partaking pathologically of the character of a genuine tumour. This tumour originates in the endothelium of the lymphatics, whose cells assume in consequence a well-defined and peculiar character, and which are distinguished pre-eminently by a strikingly marked fatty content never arising in antecedent degenerative processes.

FINIS.

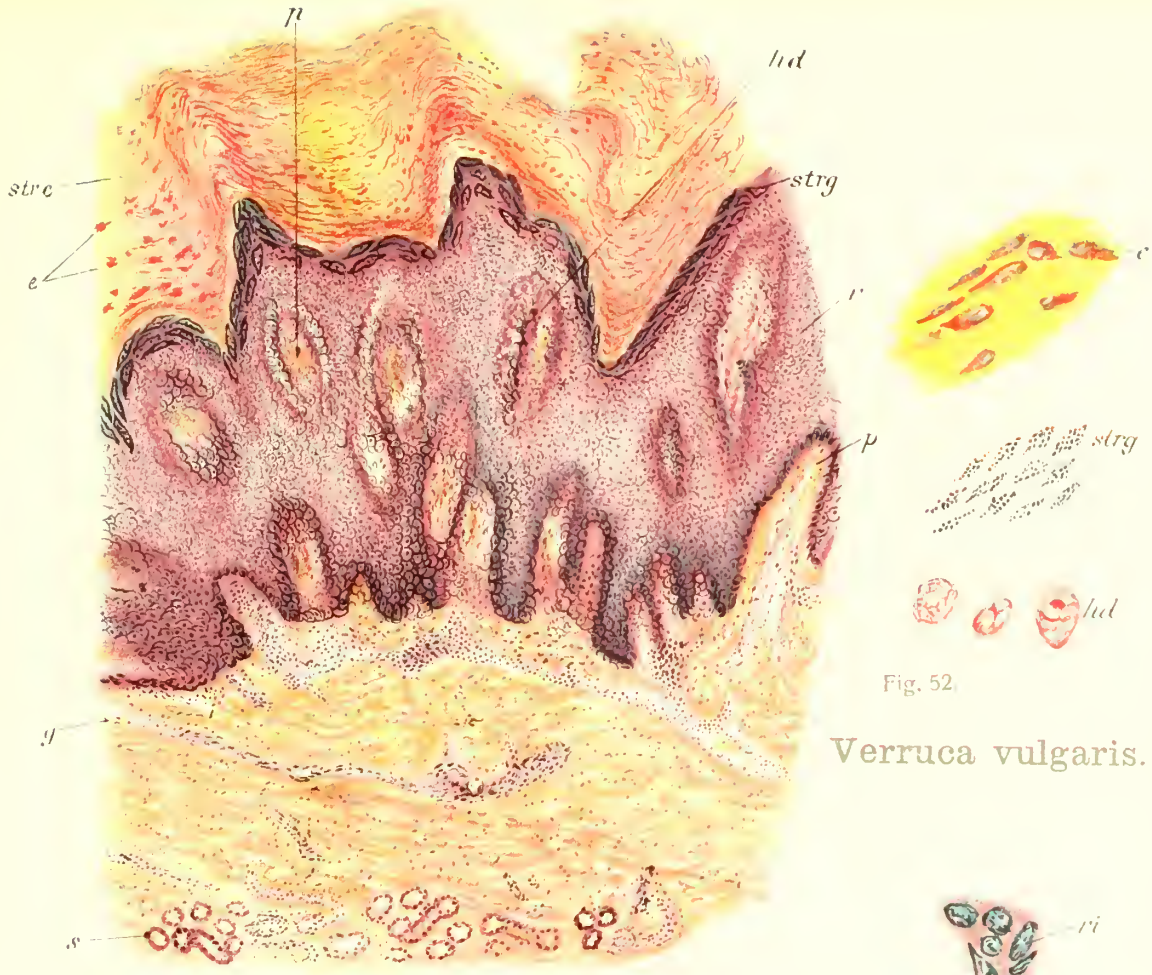


Fig. 52.

Verruca vulgaris.

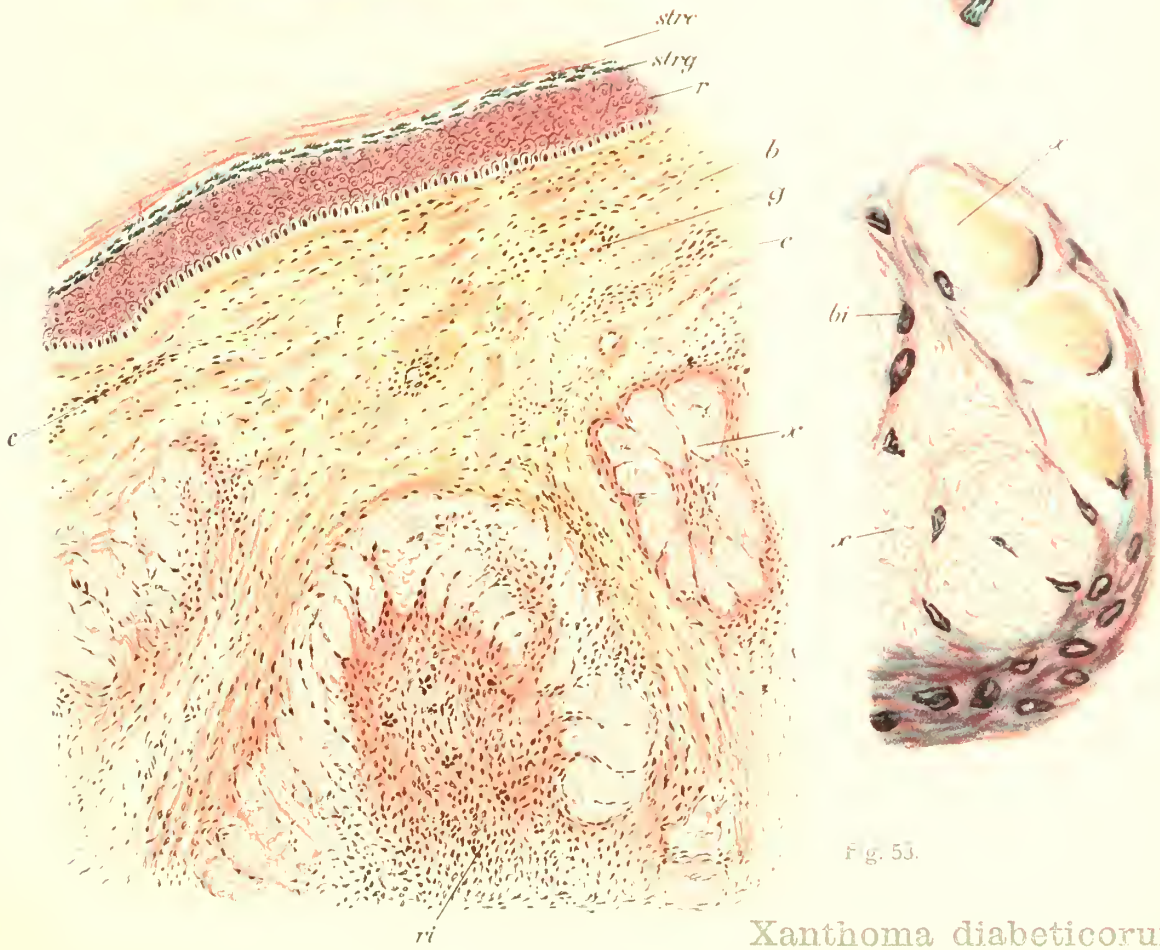


Fig. 53.

Xanthoma diabeticorum.